AR201-13468

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VICE PRESIDENT
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American Chemistry Council *Good Chemistry Makes It Possible*

December 14, 2001

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P. O. Box 1473
Merrifield, VA 22116

RE: Phthalate Esters Panel Test Plans for Phthalate and Trimellitate Esters; HPV registration number

Dear Ms. Whitman:

The Phthalate Esters Panel HPV Testing Group of the American Chemistry Council submits its test plans for Phthalate and Trimellitate Esters under the High Production Volume (HPV) Challenge Program. However, they are not volunteered in the HPV program, because they are described in the test plans and noted here for information purposes and are already part of the OECD SIDS program.

Chemical Name	CAS Number
1,2-benzenedicarboxylic acid, dibutyl ester	84-74-2
1.2-benzenedicarboxylic acid, butylbenzyl ester	85-68-7
1,2-benzenedicarboxylic acid, di(2-ethylhexyl)ester	117-81-7
1,2,4-benzenetircarboxylic acid, tris (2-ethylhexyl) ester	3319-31-1
1,2-benzenedicarboxylic acid diisononyl ester	28553-12-0
1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9 rich	68515-48-0
1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10 rich	68515-49-1

Thus, data presentation and any needed testing for these seven chemicals will occur through the OECD program. The Phthalate Esters Panel HPV Testing Group will, where appropriate, use these chemicals for data read across purposes.

In preparing this test plan, the Panel has given careful consideration to the principles contained in the letter EPA sent to all HPV Challenge Program participants on October 14, 1999. As requested by EPA in that letter, the Panel has sought to maximize the use of scientifically appropriate categories of related chemicals and of structure activity relationships. Additionally, and also as requested in EPA's letter, in analyzing the adequacy of existing data, the Panel has conducted a thoughtful, qualitative analysis rather than use a rote checklist approach. The Panel has taken the same thoughtful approach when developing this revised test plan and believes it conforms to those principles.

If you have any questions, please call Marian Stanley, Manager Phthalate Esters Pane,l at (703-741-5623), e-mail Marian_Stanley@americanchemistry.com.

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AR201-13468A

HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For The Trimellitate Category

Prepared by:

ExxonMobil Biomedical Sciences, Inc.

For The

Phthalate Esters Panel HPV Testing Group of the American Chemistry Council

December 13, 2001

THE PHTHALATE ESTERS PANEL

The American Chemistry Council Phthalate Esters Panel sponsoring this test plan includes the following member companies:

Eastman Chemical Company
ExxonMobil Chemical Company
Sunoco Chemicals
Teknor Apex Company

TRIMELLITATE CATEGORY

CAS Number	CAS Number Description
3319-31-1	1,2,4-benzenetricarboxylic acid, tris (2-ethylhexyl) ester
27251-75-8	1,2,4-benzenetricarboxylic acid, triisooctyl ester
53894-23-8	1,2,4-benzenetricarboxylic acid, triisononyl ester
67989-23-5	1,2,4-benzenetricarboxylic acid, decyl octyl ester

PLAIN ENGLISH SUMMARY

The trimellitates category contains four U.S. HPV trimellitates. These substances are 1,2,4 benzenetricarboxylic acids with side chain esters ranging from C8-C10. Of these, the one most extensively tested, Tris-2(ethylhexyl) trimellitate (TOTM), has been shown to have a low order of toxicity. Existing toxicology data on these substances were supplemented with information on phthalate esters (1,2 benzenedicarboxylic acids) with side chains of similar length.

The American Chemistry Council Phthalate Esters Panel HPV Testing Group believes that there is a sufficient amount of information available on trimellitates to substantially characterize the human health effects and environmental fate and effects endpoints for the remaining members of this category under the HPV program. TOTM has been sponsored under the OECD SIDS program through ICCA. A full SIDS data set exists for TOTM and is being used to support the hazard assessment of the remaining trimellitates in this category. No additional toxicology tests are proposed for these materials.

EXECUTIVE SUMMARY

The American Chemistry Council Phthalate Esters Panel HPV Testing Group and its member companies hereby submit for review and public comment the test plan for the Trimellitate category under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program (Program). It is the intent of the Phthalate Esters Panel and its member companies to use existing data and scientific judgment/analyses to meet the requirements of the Screening Information Data Set (SIDS) for human health, environmental fate and effects, and physical/chemical properties for this category.

This test plan addresses the 4 HPV trimellitates listed in Table 1. Trimellitates are produced by esterification of trimellitic anhydride (TMA) with various linear and branched alcohols in the presence of an acid catalyst to form 1,2,4 –benzenetricarboxylic acids. Because the side chains for all substances in this category are of similar carbon number (C8-C10) and structure, all four of the HPV substances were grouped into a single category.

Trimellitates are used predominantly as plasticizers for production of flexible PVC. Because of their relatively high molecular weight (>500 g/mole) and bulky structure, they have lower volatility and greater resistance to migration than the corresponding phthalate ester plasticizers. They are predominantly used in the manufacture of high temperature PVC cables (Wilson, 1996). Since these chemicals are produced in closed systems, there is essentially no occupational exposure to these substances except at the flexible PVC production facility. Usually, these substances have been already blended to the compound as plasticizer, so it is not expected that downstream users or consumers are directly exposed to trimellitates.

Testing Rationale:

Because of the similarity in chemical structure, the Panel believes that the toxicological properties of the substances in this category will be similar as well. Thus, the Panel considers that the data for the best tested member of this category, tris-2(ethylhexyl) trimellitate (TOTM), also represent the potential for human and environmental effects of the other members of this category. In addition, data on TOTM indicate that it is hydrolyzed very poorly in rodents to the di-2-ethylhexyl ester and a mono-2-ethylhexyl ester. Therefore, "read across" for trimellitates would consist of comparisons to the similar phthalate esters, which are also being sponsored by the Panel under the HPV program. Existing toxicology data on these substances were supplemented with information on phthalate esters (1,2 benzenedicarboxylic acids) with side chains of similar length (see test plan for phthalate esters category).

TOTM has been sponsored by Japan under the OECD SIDS program. A review of the available data for TOTM (Table 2) indicates that all endpoints have been adequately addressed, and that TOTM exhibits a low order of toxicity. Further, a comparison of the relative toxicity of TOTM to its corresponding phthalate ester, di-ethylhexyl phthalate

(DEHP), indicates that trimellitates are much less active than phthalate esters with side chains of similar length. Due to their higher molecular weight and bulky side chains, the remaining members of this category are expected to demonstrate a lower order of toxicity than TOTM. This is supported by a similar structural-activity relationship observed with phthalate ester compounds, i.e., the higher molecular weight phthalates (ester side chains $\geq$C7) are less active that the transitional phthalates (ester side chains C4-C6). Thus, the use of TOTM to represent the potential hazards of the other category members is a conservative position. No additional toxicity tests are proposed for this category.

TEST PLAN FOR THE TRIMELLITATE CATEGORY

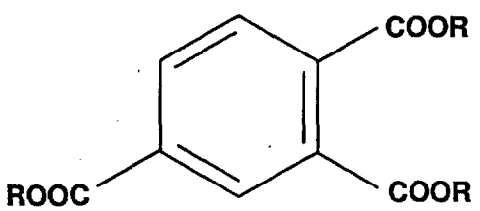
INTRODUCTION

The American Chemistry Council Phthalate Esters Panel HPV Testing Group and its member companies have committed voluntarily to develop screening level human health effects, environmental fate and effects, and physicochemical data for the trimellitates category under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program.

This plan identifies CAS numbers used to characterize the SIDS endpoints for this category, identifies existing data of adequate quality for substances included in the category, and provides the Panel's rationale for utilizing the available SIDS data to characterize the potential hazards of all category members. The objective of this effort is to identify and adequately characterize the physicochemical properties along with human health, environmental fate and effects, to satisfy the EPA HPV program.

DESCRIPTION OF THE TRIMELLITATES CATEGORY

The trimellitates comprise a family of chemicals synthesized by esterifying trimellitic anhydride with alcohols with average carbon numbers ranging from approximately C7-C10, in the presence of an acid catalyst. The category includes the four trimellitates listed in Table 1. Trimellitates in this category are all 1,2,4-benzenetricarboxylic acids with side chain ester groups ranging from C8 to C10. The structural formula for trimellitates varies somewhat depending on the isomeric composition of the alcohols used in their manufacture. The specific alcohols used are 2-ethylhexanol (TOTM), iso-octyl alcohol (TIOTM), iso-nonyl alcohol (TINTM), and a mixture of linear and branched decyl (40%) and octyl (60%) alcohols (DOTM).



Trimellitates are colorless to slightly yellow liquids with high boiling points (> 250°C) and low vapor pressures; these properties contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils, but essentially insoluble in water. Because of the similarity in structure as well as physicochemical properties, the trimellitates were grouped into a single category containing four substances with carboxylic side chain ester groups ranging from C8-C10.

DATA ADEQUACY REVIEW

Literature Search:

Literature searches were conducted by EMBSI Information Services on the environmental and mammalian toxicity endpoints for four trimellitates using the CAS numbers supplied by the Phthalate Esters Panel. A review of these substances was recently published (David et al., 2001). Therefore, the search was conducted using the MEDLINE and TOXLINE databases and limited to studies published since 1995. The TSCATS database was searched for relevant unpublished studies on these chemicals. In addition, a complete SIDS information package on TOTM was kindly provided by Dainippon Ink & Chemicals, Japan, as part of it's OECD SIDS submission. Standard handbooks and other reference material (CRC Handbook on Chemicals; IUCLID) were consulted for physical/chemical properties. Information on manufacture and use was taken from EPA (1981) and Wilson (1996).

In addition, modeled data were entered into the robust summaries for all of the physical properties. There are a number of reasons for this approach:

- The EPA guidance (www.epa.gov/opptintr/chmrtk/robsumgd.htm) allows inclusion of calculated values in the robust summaries for physical/chemical elements,
- The need for a complete set of physical property data in order to calculate environmental distribution, and
- Supplement measured physical properties for these trimellitates.

The physical properties were modeled using the SRI/EPA computer program EPIWIN, a modeling package that includes a number of algorithms developed at or for the EPA. EPIWIN is the program used and advocated by the EPA. Because the model is a structure-property model a specific discrete structure is required and EPIWIN contains a CAS number database which contains the structures for the chemicals. For mixtures, a single representative structure is contained in the database and in this work, these surrogate chemical structures were accepted for further modeling. It should be remembered that the resultant physical properties are for a single structure not a mixture so the values are discrete numbers rather than ranges.

The existing data for environmental and mammalian toxicology endpoints were reviewed using the literature searches to identify the most relevant studies for each chemical in the group. A number of the listed individual chemicals had no relevant studies identified in the searches. For the listed chemicals for which there were relevant data, all studies were reviewed using the criteria outlined in the EPA's method for determining the adequacy of existing data for the HPV program and the ranking system proposed by Klimisch et al. (1997). A list of the most relevant studies that were available for environmental and mammalian health endpoints is presented in **Appendix 1.**

Studies that were chosen for robust summaries represented the best available data for each specific endpoint. Published studies from the general literature, as well as a number of unpublished company reports, were obtained and summarized. Some endpoints include multiple summaries in order to present a more complete data set.

TESTING RATIONALE

Overview:

The trimellitates category contains four U.S. HPV trimellitates. These substances are 1,2,4 benzenetricarboxylic acids with side chain esters ranging from C8-C10. Of these, the one most extensively tested, TOTM, will be used as a representative chemical to assess the potential environmental and health effects of the other trimellitate category members. A review of the available data for TOTM (Table 2) indicates that all endpoints have been adequately addressed, and that TOTM exhibits a low order of toxicity. Due to their higher molecular weight and bulky side chains, the remaining members of this category are expected to demonstrate a lower order of toxicity than TOTM. This is supported by a similar structural-activity relationship observed with phthalate ester compounds, i.e., the higher molecular weight phthalates (ester side chains $\geq$C7) are less active than the transitional phthalates (ester side chains C4-C6). Thus, the use of TOTM to represent the potential hazards of the other category members is a conservative position. No additional toxicity tests are proposed for this category.

Manufacturing and Use

Trimellitates are produced by esterification of trimellitic anhydride (TMA). The basic structure is an aromatic ring with side chains in the 1, 2 and 4 positions. Trimellitate plasticizers are based on alcohols with (average) carbon numbers in the range 7-9. The relatively high molecular weight and bulky structure of these molecules gives them low volatility and makes them relatively resistant to migration. Their main application is in high temperature PVC cables (Wilson, 1996).

Category Justification

The four trimellitates in the HPV category, tris-2(ethylhexyl) trimellitate (TOTM), tri-isooctyl trimellitate (TIOTM), tri-isononyl trimellitate (TINTM) and decyl,octyl – trimellitate (DOTM). The distinguishing feature of these substances is in the alcohol side chains. TOTM has side chains with a 2-ethylhexyl moiety, TIOTM has iso-octyl side chains, TINTM has isononyl side chains and DOTM has mixed decyl (40%) and octyl (60%) side chains. These molecules are of the same general structure, differing only in side chains, and the side chains themselves are very similar, containing carbon numbers ranging from C8 to C10. These molecules also have similar physical and chemical properties; in particular because of their high molecular weights and aliphatic character,

they have very low vapor pressures and very low water solubilities. Because of the similarity in structure and physical/chemical properties, the Panel believes that it is reasonable to consider this group of substances as a category and to rely on data for one representative member (TOTM) for all other representatives in this category.

Physicochemical Properties

Physicochemical properties for trimellitates are shown in Table 2A. The 2-ethylhexyl trimellitate ester (TOTM) is representative of this group of trimellitates as the other members are quite similar triesters of mellitic acid with C8 through C10 alcohols. TOTM has a melting point of -46°C and a boiling point of >300°C at 1 atmosphere (measured values are >300°C at reduced pressure). Vapor pressure measurements are only possible for TOTM at very high temperatures due to its low order of volatility. Measured values are <1 Pa at 100°C and 13 Pa at 200°C; thus, the vapor pressure at 25°C is extrapolated to be < 0.01 Pa. The vapor pressure calculated for TOTM by EPIWIN is $5x10^{-9}$ Pa. The water solubility of TOTM is also quite low. A measured value of $4x10^{-4}$ mg/L is available. However, water solubility is difficult to measure at such low concentrations, particularly for esters with densities near that of water and which tend to form dispersions in water and for that reason, standard test methods tend to over-estimate water solubility. The EPIWIN calculated water solubility value for TOTM is $4.5x10^{-8}$ mg/L. The log of the octanol/water partition coefficient (log K_{ow}) for TOTM is calculated (EPIWIN) as 11.6. Measured values of 5.94 and 4.35 are also available.

Structure-property modeling has been done using the EPIWIN program recommended by EPA.[1] This modeling has been used to estimate all of the required physicochemical parameters of all four of these HPV trimellitates. TOTM has a melting point below 0°C; it is expected that the other members of this group will have melting points below 0°C as well. Due to their high molecular weight, these trimellitates are expected to boil at a much higher temperature than TOTM and than the corresponding phthalate esters all of which boil at >300°C at atmospheric pressure. EPIWIN estimates boiling points >500°C for all four trimellitates. Thus, all boiling points are assuredly >300°C and measurement is not necessary.

For the phthalate esters, the EPIWIN model agrees well with measured values for the critical environmental fate properties of octanol-water partition coefficient, water solubility, and vapor pressure. By analogy with the phthalates and by EPIWIN calculations, these trimellitates are expected to be virtually water insoluble <1 part per billion) and non-volatile (~10^{-9} Pa). Measured values on TOTM confirm the expected low water solubility and vapor pressures. The log K_{ow} values for all four trimellitates are calculated to be in the range of 11 to 13. The measured values reported for TOTM seem quite unlikely, since the measured value for the corresponding phthalate diester (DEHP) is 7.7 (which agrees well with the calculated value) and TOTM is expected to be much more hydrophobic due to the presence of a third ester group. Moreover, these measured values are more than 5 orders of magnitude lower than the calculated value.

[1] US EPA (2000). The Use of Structure Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program, http://www.epa.gov/opptintr/chemrtk/sarfinl1.htm

The physical properties of vapor pressure and water solubility of the trimellitates are too low to measure accurately, as evidenced by the data for TOTM. Similarly the calculated log K_{ow} values are likely to be more accurate than laboratory measurements, due to high values beyond the range of applicability of the test methods. The water solubility is also so low as to make hydrolysis rate studies untenable. Thus, no further measurements of the physical properties of the trimellitates is necessary as the values calculated by QSAR models are likely to be as reliable or more reliable than the measured values.

Environmental Fate

There are data available on the degradability of TOTM. The measured abiotic degradation (hydrolysis) half-life of TOTM at pH 7 and 25°C is 17.5 days (0.05 year). The EPIWIN calculated hydrolysis half-life is 0.32 year. The atmospheric degradation half-life (hydroxyl radical attack) calculated by EPIWIN (AOP module) is 0.33 day. The measured biodegradability data on TOTM are an inherent 28 day degradation of 68% by ^{14}C-TOTM loss in a shake flask test and a degradation of 4.2% in the Japanese MITI test (OECD 301C, ready biodegradability). Since the phthalate esters are readily biodegradable, it is likely that the low result in the MITI test is due to lack of bioavailability since that test has a relatively high solids content and since TOTM is much less soluble than the corresponding phthalate diester (DEHP). By analogy with the phthalates, degradation of the trimellitates is expected to proceed through step-wise hydrolysis of the ester groups to free alcohol and mellitic acid. These metabolites, in turn, are known to be rapidly degraded. No further degradation testing is necessary.

The calculated environmental distribution of TOTM (Mackay level 1) indicates that negligible fractions of TOTM will partition to air or water, with the major fractions partitioning to soil (97.82%) and sediment (2.17%). Due to closely similar physical properties, exactly the same environmental distribution is calculated for the other trimellitates in this group. Environmental fate properties are shown in Table 2A.

Toxicokinetics and Metabolism

Absorption and metabolism were studied for TOTM administered in corn oil by gavage in a single dose of 100 mg/kg of body weight in 4 male SD rats. Urine and feces were collected over the following 144 hour period, after which animals were sacrificed and residual carcass levels determined. About 75% of the dose was excreted in the feces, 16% in the urine as metabolites and 1.9% was expired as $^{14}CO_2$. Radioactivity was mostly excreted in the feces as unchanged TOTM (85% of the fecal radioactivity), with 6% as isomers of the diester and 1% as the mono-2-ethylhexyl trimellitate (MEHT). Metabolites in the urine were identified as MEHT and metabolites of 2-ethylhexanol. Less than 0.6% of the dose remained in the tissues. Elimination of $^{14}CO_2$ was biphasic with half-lives of 4.3 and 31 hrs, and excretion of radioactivity in the urine was biphasic with half-lives of 3.4 hrs and 42 hrs. (Eastman Kodak Company, unpublished report 1984).

These data indicate that TOTM is poorly hydrolyzed and absorbed across the gastrointestinal tract. By comparison, numerous absorption and metabolism studies on DEHP indicate that DEHP is readily hydrolyzed in the gut prior to absorption, with ~50% of the DEHP dose absorbed by rodents following oral administration (Albro and Lavenhar, 1989). Hydrolysis in the gut appears to be an obligatory step for systemic absorption of phthalate esters. Thus, the relatively poor hydrolysis and systemic absorption of TOTM may in part explain the observed lower toxicity of trimellitates as compared to phthalate esters.

Mammalian Toxicity Data

A summary of the available toxicity data on trimellitates is shown in Table 2B.

Acute Toxicity

TOTM exhibits very limited acute toxicity with an oral LD_{50} > 2 g/kg, a dermal LD_{50} > 20 ml/kg (approximately 20 g/kg), and an acute inhalation LC_{50} in the range of 0.23 to 2.64 mg/L (nominal). There is, in addition, an acute oral LD_{50} value for TINTM of > 10 g/kg. Although some of these data are from older studies that may not have been fully consistent with current guidelines, these results are consistent with those from studies of phthalate esters produced from similar alcohol feedstocks. These data indicate that acute toxicity is not a concern for molecules of this type. No additional acute toxicity testing is planned for this category.

Repeated Dose Toxicity

TOTM was tested for repeated dose toxicity in rats. Exposure was by dietary administration at levels of 0.2, 0.67, and 2.0%. There was no effect on body weight or food consumption; liver weights in the 0.67% group were significantly increased, but this was judged to have been a spurious finding as liver weights were not increased in the 2.0% group. There was also evidence of increased metabolic enzymes and cholesterol. There were also some changes in blood parameters but these were inconsistent, and were judged to be without toxicological consequence. The NOAEL was 654 mg/kg/day based on a finding of slight peroxisome proliferation at the top dose (2%, ca. 1826 mg/kg/day). A NOAEL of 1000 mg/kg/day was similarly reported in an unpublished 28 day oral feeding study in rats (Japan Ministry of Health & Welfare, 1996). Based on these data, no additional subchronic toxicity testing is planned for this category.

Mutagenicity

TOTM was not mutagenic in Salmonella and did not cause mutations in the HGPRT assay in CHO cells. Additionally, there was no increase in unscheduled DNA synthesis in rat hepatocytes. TOTM induced neither structural chromosomal aberrations nor polyploidy in CHL/IU cells up to the limit concentration of 5.0 mg/ml, in the absence or presence of an exogenous metabolic activation system. In addition, a wide range of phthalate esters produced from similar C8-C10 alcohol feedstocks have been evaluated

for both point mutations (Zeiger et al., 1987; Barber et al., 2000) and chromosomal aberrations (McKee, 2000) and have consistently been found to be inactive. Based on these data there is no need to conduct additional tests of trimellitates for point mutations or chromosomal aberrations.

Reproductive/Developmental Toxicity

TOTM was studied for oral toxicity in rats in an OECD preliminary reproduction toxicity screening test at doses of 0, 100, 300 and 1000 mg/kg/day. Histopathological examination of the testes revealed decreases in spermatocytes and spermatids in males of the 300 and 1000 mg/kg groups. No effects of TOTM were detected on general appearance, body weight, food consumption, autopsy findings, and weights of the reproductive organs of both sexes, or on histopathological examination of the ovary. Except for the effects in males observed on histopathological examination, no influence of TOTM was detected regarding reproductive ability, organ weights or histopathological appearance of the ovaries, delivery or maternal behavior of dams. No effects of TOTM were detected on viability, general appearance, body weight or autopsy findings of offspring. On the basis of these findings, the NOELs of TOTM for reproductive/developmental effects were considered to be 100 mg/kg/day for males, 1000 mg/kg/day for females, and 1000 mg/kg/day for offspring.

A comparison of TOTM to DEHP indicates that TOTM is considerably less active than its diester analog. The LOAEL for DEHP-induced reproductive and developmental effects is 140 mg/kg/day and 750 mg/kg/day, respectively. In contrast, no reproductive or developmental effects were observed with TOTM at dose levels up to 1000 mg/kg/day.

Phthalate esters produced from similar C8-C10 alcohol feedstocks as used to produce trimellitates have also been extensively studied for potential reproductive and developmental effects. Phthalate esters with linear alkyl chains $\geq$C7 (High molecular weight phthalates), demonstrate neither reproductive nor developmental effects in rodents. Thus it is highly unlikely that the remaining trimellitates in this category will exhibit any reproductive or developmental effects. No further reproductive or developmental testing is proposed for this category.

Environmental Toxicity

A summary of the available toxicity data on trimellitates is shown in Table 2B. There are acute aquatic toxicity data available for TOTM in fish daphnia and algae. No acute toxic effects to fish (*Oryzias latipes*) were observed at the highest concentration tested (100 mg/L, NOEC > 100 mg/L). Similarly, no effects were observed in algae (*Selenastrum capricornutum*) at 100 mg/L (NOEC > 100 mg/L). The EC_{50} for *Daphnia magna* was also above the highest concentration tested (180 mg/L). It should be noted that all of these toxicity tests were conducted at concentrations many orders of magnitude higher than the true water solubility of TOTM through the use of a chemical dispersants. The calculated values for TOTM acute toxicity also predict no effects at the limit of water

solubility. Chronic fish and daphnia exposure studies on TOTM also show no toxicity at and above its water solubility limit.

No measured aquatic toxicity data are available for the remaining members of this category. However, all of these are similar in structure to TOTM and to the higher phthalates and are expected to have the same characteristic aquatic toxicity, namely none. They are even less water soluble than the higher phthalates and like the higher phthalates, their solubility is too low to result in toxicity to aquatic organisms.

In addition, quantitative structure activity relationships (QSARs) are acceptable sources of ecotoxicity information for the evaluation for chemicals that belong to chemical classes with established QSARs.[2] Esters are such a class and the EPA's QSAR model "ECOSAR" may be relied upon to evaluate the potential aquatic toxicity of these trimellitate esters. No additional environmental testing is proposed for this category.

TEST PLAN SUMMARY

The American Chemistry Council Phthalate Esters Panel HPV Testing Group believes that there is a sufficient amount of information available on TOTM to substantially characterize the human health effects and environmental fate and effects endpoints for the remaining members of this category under the HPV program.

Physicochemical properties and environmental fate for all category members were calculated using appropriate QSAR models, and supplemented with measured data from the literature. Due to the poor solubility of these materials, the values calculated by QSAR models are likely to be as reliable or more reliable than the measured data.

Mammalian toxicity data on TOTM is being used to characterize the potential hazards of the remaining category members. Sufficient SIDS data exists on TOTM to reliably assess acute toxicity, repeat dose toxicity, point mutations, chromosomal aberrations, and reproductive toxicity. The developmental effects of TOTM were indirectly measured in an OECD preliminary reproduction toxicity screening test. Extensive reproductive and developmental studies on phthalate esters were used as supportive information to characterize these endpoints.

Both calculated and measured values for TOTM environmental toxicity endpoints predict no effects at the limit of water solubility. As the remaining trimellitates are even less water-soluble than TOTM, their solubility is too low to result in toxicity to aquatic organisms.

No additional toxicology tests are proposed for these materials.

Table 1. CAS Numbers and Descriptions

[2] US EPA (2000). The Use of Structure Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program, http://www.epa.gov/opptintr/chemrtk/sarfinl1.htm.

CAS Number	CAS Number Description	Acronym
3319-31-1	1,2,4-benzenetricarboxylic acid, tris (2-ethylhexyl) ester	TOTM
27251-75-8	1,2,4-benzenetricarboxylic acid, triisooctyl ester	TIOTM
53894-23-8	1,2,4-benzenetricarboxylic acid, triisononyl ester	TINTM
67989-23-5	1,2,4-benzenetricarboxylic acid, decyl octyl ester	DOTM

Table 2. Summary of SIDS Information on Trimellitates
A. Physical/Chemical Properties of Trimellitates

(R) Carbon Chain Length	CAS Number	Chemical Name	MP* (°C)	BP** (°C)	VP (hPa@25°C)	PC (log Pow)	Water Solubility (mg/L @25°C)	Photodeg Half-life (days)	Hydrolysis Half-life (yrs)	Transport (%) c			
										Soil	Air	Water	Sediment
C8	3319-31-1	tris 2-ethylhexyl (TOTM)	-46 97 c	>300 541 c	<0.0001*** 5.25E-11 c	5.94 11.59 c	3.9E-04 4.51E-08 c	0.33 c	0.05 0.32 c	97.8	3.6E - 6	2.8E - 7	2.17
C8	27251-75-8	triisooctyl ester	<0 197 c	541 c	5.25E-11 c	11.59 c	4.51E-08 c	0.35 c	0.43 c	97.8	3.64E - 6	2.8E - 7	2.17
C9	53894-23-8	triisononyl ester	<0 224 c	>300 575 c	3.17E-12 c	13.06 c	1.32E-09 c	0.31 c	0.86 c	97.8	2.74E - 7	9.61E -9	2.17
C8,C10	67989-23-5	decyl, octyl ester	<0 234 c	585 c	1.37E-12 c	12.79 c	2.78E-09 c	0.32 c	0.98 c	97.8	1.02E - 7	1.79E - 8	2.17

c = calculated data using EPWIN; all other values are derived from measurements

* = All of these trimellitates are liquids at zero degrees C. Modeled data do not accurately reflect melting points for these substances

** = Measured boiling points were determined to be >300°C at 0.66 kPa

*** = vapor pressure of TOTM 13 Pa @ 200°C

Table 2. Summary of SIDS Information on Trimellitates
B. Toxicology Data on Trimellitates

(R) Carbon Chain Length	CAS Number	Chemical Name	Acute Oral LD50	Acute Dermal LD50	Acute Inhalation LC50	Repeated Dose Toxicity	GeneTox (Ames)	GeneTox (Chrom. Abs.)	Toxicity to Reproduction	Developmental Toxicity / Teratogenicity	Acute Fish (A) mg/L	Daphnia (B) mg/L	Algal (C) mg/L	Biodegradation %
C8	3319-31-1	tris 2-ethylhexyl (TOTM)	> 3.2 g/kg (rat, mouse)	>20 ml/kg (guinea pig) >2.0 ml/kg (rabbit)	<2.64 mg/L (rat, nominal)	NOAEL (rat, dietary) 654 mg/kg/day	Negative	Negative (CHL/IU cells)	NOAEL (rat, oral) 1000 mg/kg/day	NOAEL (rat, oral) 1000 mg/kg/day (3)	>100	>180	>100	68-71 (1) 4.2 (2)
C8	27251-75-8	Triisooctyl ester	R	R	R	R	R	R	R	R	R	R	R	R
C9	53894-23-8	Triisononyl ester	> 10 g/kg (rat)	R	R	R	R	R	R	R	R	R	R	R
C8, C10	67989-23-5	decyl, octyl ester	R	R	R	R	R	R	R	R	R	R	R	R

R = read-across to TOTM

Footnotes: A) Japanese Medaka (*Oryzias latipes*), 96 hr LC50 & NOEC
B) *Daphnia magna*, 48-hr EC50
C) *Selenastrum capricornutum*, 72-hr EC50 & NOEC

(1) Inherent biodegradation by Shake Flask Method
(2) Ready biodegradation by MITI method (OECD 301C)
(3) OECD Preliminary reproduction toxicity screening test; indirect measure of develomental effects

References*

Albro, P.W. and S.R. Lavenhar (1989). Metabolism of di(2-ethylhexyl)phthalate. Drug Metabolism Reviews, 21(1): 13-34.

Wilson, A., (1996). Plasticizers – Selection, Applications and Implications. Rapra Review Reports 8:15-16.

EPA (1981). Chemical Technology and Economics in Environmental Perspective. Task VI. A survey of plasticizers, epoxies, linear polyesters, and trimellitates. Prepared for Environmental Protection Agency by Midwest Research Inst. EPA

Klimisch, H. J., M. Andreae, and U. Tillmann. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regulatory Toxicol. and Pharmacol. 25:1-5.

CRC Handbook of Chemistry and Physics, 81st editing (2000). CRC Press LLC, Boca Raton, FL.

US EPA (2000). The Use of Structure Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program, http://www.epa.gov/opptintr/chemrtk/sarfinl1.htm

*The list of references is not a comprehensive bibliography of all of the trimellitate literature, merely a series of papers that illustrate key points made in the text. The information in these papers also supplements the robust summaries developed for toxicology studies of listed substances in tests addressing specific SIDS endpoints.

Appendix 1: Literature Search

3319-31-1 1,2,4-benzenetricarboxylic acid, tris (2-ethylhexyl)ester

Reviews

Japan dossier and robust summary for tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate. (DRAFT unpublished report, 2001).

Japan Ministry of Health & Welfare (1996). Toxicity Testing Reports of Environmental Chemicals, Vol. 4. http://wwwdb.mhlw.go.jp/ginc/dbfile1/file/file3319-31-1.html.

David, R. et al., (2001). Esters of aromatic mono-, di-, and tricarboxylic acids, aromatic diacids and di-, tri-, or polyalcohols. In: Patty's Toxicology, Fifth edition, Vol. 6, Bingham E., B. Cohrssen and C.H. Powell (eds.), John Wiley & Sons, Inc. pp. 635-932.

Environmental and Health Assessment of Alternatives to Phthalates and to Flexible PVC (2001). Danish EPA, Environmental project No. 590.

Phys/Chem Data

IUCLID, International Uniform Chemical Information Database, European Chemicals Bureau, Ispra, Italy - Feb 2000.

Japan dossier and robust summary for tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate. (DRAFT unpublished report, 2001).

Ecotoxicity Data

Japan dossier and robust summary for tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate. (DRAFT unpublished report, 2001).

Mammalian Toxicity

BIBRA, The British Industrial Biological Research Association. (1985). 28-day toxicity study with tri(2-ethylhexyl)trimellitate in the rat. Report to the Chemical Manufacturers Association. Report No. 0496/1/85.

Eastman Kodak Company, Rochester NY (1971). Tri(2-ethylhexyl)trimellitate. Acute oral toxicity. Unpublished report.

Eastman Kodak Company, Rochester NY (1971). Tri(2-ethylhexyl)trimellitate. Acute dermal toxicity. Unpublished report.

Eastman Kodak Company, Rochester NY (1984). Absorption and Metabolism of (hexyl-2-^{14}C)tris-(2 ethylhexyl) trimellitate in the rat. OTS 42040. Doc. ID 408465031.

Eastman Kodak Company, Rochester NY (1971). Tri(2-ethylhexyl)trimellitate. Acute inhalation toxicity. Unpublished report.

Japan Ministry of Health & Welfare (1996). Toxicity testing Reports of Environmental Chemicals, Vol. 4. http://wwwdb.mhlw.go.jp/ginc/dbfile1/file/file3319-31-1.html.

Zeiger, E., B. Anderson, S. Haworth, T. Lawlor and K. Mortelmans. (1988). Salmonella mutagenicity tests. IV. Results from the testing of 300 chemicals. *Environmental and Molecular Mutagenesis* **11**(12):1-158 .

27251-75-8 1,2,4-benzenetricarboxylic acid, triisooctyl ester

No relevant studies found.

53894-23-8 1,2,4-benzenetricarboxylic acid, triisononyl ester

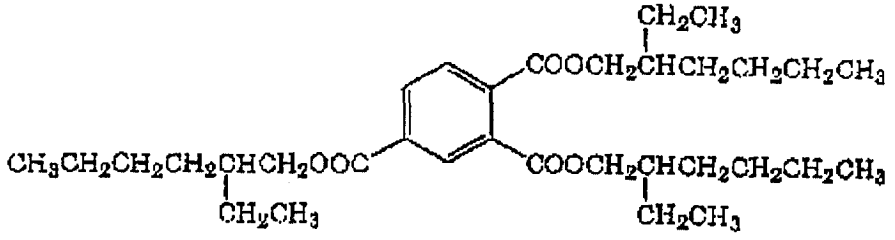
Esso Research and Engineering Company (1969). Acute Oral Administration of MRD-69-31 in Rats. Unpublished Report.

67989-23-5 1,2,4-benzenetricarboxylic acid, decyl octyl ester

No relevant studies found.

AR201-13468B

SIDS INITIAL ASSESSMENT PROFILE

CAS NO.	3319-31-1
CHEMICAL NAME	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
Structural formula	

RECOMMENDATION

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human health

Acute toxicity of TOTM is low, LD_{50} >2,000 mg/kg in rats. In the irritation-test for animals, this substance is slightly irritating to the skin and the eyes. Sensitization test on guinea pig showed"no sensitization". Oral study in rats conducted for 28 days at doses of0(0), 0.2(184), 0.67(650), 2.0(1826) % (mg/kg bw/day) of TOTM. There were no statistically significant differences in body weights between control andTOTM treated groups. There was a significant difference between control and treated groups in thefollowing: hemoglobin concentration (lower in both sexes, 0.67 or 2.0% TOTM), leucocyte counts (higher in males at 0.67 or 2.0%), absolute and relative liver weights (higher in both sexes at all levels except 0 or 0.2%),serum albumin (higher in both sexes at 0.67 or 2.0%), serum cholesterol levels (higher in males at 0.67 or 2.0%), serum urea (higher in males at 2.0%), serum lipids (decreased in females at0.2%). Liver biochemistry revealed statistically significant differences between treated and control groupsas indicated by palmitoyl CoA oxidation (increased in both sexes at 2.0% and males at all dose levels), and catalase activity (increased in males at 2.0%).

Preliminary reproductive toxicity screening test reveals moderate decrease ofspermatocytes and spermatids in males at 100mg/kg/day. From these two test results, he NOAELs for repeated oral toxicity were considered to be100 mg/kg/day for male rats. The NOAELs for reproductive/ developmental toxicity were considered to be1,000 mg/kg/day for female rats and for offspring.

TOTM was evaluated its genotoxicity by many assay systems. It was neithermutagenic in bacteria nor clastogenic in mammalian cells*in vitro*. All other *in vitro* and *in vivo* assays gave negative results. It is concluded that TOTM is not genotoxic *in vitro* and *in vivo*. The reported results of carcinogenecity was invalid.

Absorption and metabolism were studied for ^{14}C labeled TOTM and about 75% of the dose was excreted unchanged in the feces, 16% in the urine as metabolites and 1.9% was expired as $^{14}CO_2$.

Environment

The Mackay level III fugacity Model was employed to estimate the environmental distribution of TOTM in air, water, soil and sediment. If released to air, TOTM will exist solely in the particulate phase in the ambient atmosphere. If released to soil, TOTM is not expected to have mobility. If released into water, TOTM is expected to adsorb to suspended solids and sediment in water.

TOTM has to be considered as weakly toxic against aquatic organisms. The substance is not readily biodegradable. Measured BCF of this chemical is reported as less than 1 to 2.7 in carp for 6 weeks, which suggest that bioconcentration in aquatic organisms is much lower than the value estimated from logPow(=5.94). The toxicity data to aquatic plants (algae; *Selenastrum capricornutum*) was >100 mg/L for EC_{50} (72hr) and NOEC (72hr). The acute toxicity data in fish (medaka; *Oryzias latipes*) were >100 mg/L (96h, LC_{50} and NOEC) and >75 mg/L (14d, LC_{50} and NOEC). In *Daphnia magna*, acute toxicity was >180mg/L (48hr: EC_{50}) and chronic toxicity was 55.6mg/L (21d, reproduction NOEC). All these data were obtained in supersaturated solution with the aid ofsolubilizer (HCO-40). The test solution was considered to be homogeneous substantially. Another chronic toxicity data in*Daphnia magna* (NOEC >0.082mg/L) was reported. Though this value is lower than the saturation point, the observed concentration data was less reliable. Assessment factor of 100was chosen to determine the lowest PNEC. Thus, calculated PNEC (=0.00082 mg/L) of TOTM is closely to the value of one hundredths (assessment factor) of saturation point. From these toxicity data, it is difficult to decide the exact PNEC, but we are sure of the practical safety of TOTM against aquatic organisms.

Exposure

TOTM is manufactured as the plasticizer of PVC applications.
The production volume of TOTM in Japan is approximately 20,000 tonnes/year and also, there are 5 manufacturers in Japan. Estimated global production is 40,000-100,000 tonnes/year. This substance is produced in closed system and mainly used asplasticizer for PVC electrical cable and wire. And so, this substance has been already blended to the compound asplasticizer, so it is not expected that downstream users or consumers of electric wire industry may expose to this substance.

Occupational exposure may occur through dermal contact and inhalation of mist. The process is constructed by closed system and workers wear protective gloves and goggles during the operation, so significant exposure is not expected.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation

FULL SIDS SUMMARY

CAS NO: 3319-31-1		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		OECD TG 102	< - 50 °C (223 K)
2.2	Boiling Point		Other (unknown)	283 °C (at 4 hPa)
2.3	Density		Other (unknown)	0.987-0.990 g/cm^3 at 20 °C
2.4	Vapour Pressure		OECD TG 104	< 2.8 x 10^{-4} Pa at 100 °C
2.5	Partition Coefficient (Log P_{ow})		OECD TG 107	5.94 at 25 °C
2.6A.	Water Solubility		OECD TG 105	0.13 mg/L at 25 °C
B.	pH			None
	pKa			None
2.12	Oxidation: Reduction Potential			None
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation			None
3.1.2	Stability in Water		OECD TG 111	Stable at pH 4 at 50°C $T_{1/2}$=17.5 days at pH 7 at 25°C $T_{1/2}$=11.9 days at pH 9 at 25°C
3.2	Monitoring Data			None
3.3	Transport and Distribution		Calculated (Level III Fugacity Model)	(Release 100% to air) Air Water Soil Sediment 19.6% 4.7% 66.2% 9.5% (Release 100% to water) Air Water Soil Sediment 0.0% 32.7% 0.1% 67.2% (Release 100% to soil) Air Water Soil Sediment 0.0% 0.0% 100% 0.0%
			(local exposure)	PEC_{local} = None
3.5	Biodegradation		OECD TG 302C	4.2 % after 28 days
3.7	Bioaccumulation		OECD TG 305C	BCF=1-2.7(Conc. 0.2 mg/L)
ECOTOXICOLOGY				
4.1 A	Acute Toxicity to Fish	*Oryzias Latipes* *Oryzias latipes*	OECD TG 203	LC_{50} (96 hr) > 100 mg/L
4.1 B	Prolonged Toxicity to Fish		OECD TG 204	LC_{50} (14 day) > 75 mg/L NOEC(14 day) > 75 mg/L LOEC(14 day) > 75 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24 hr) > 180 mg/L EC_{50} (48 hr) > 180 mg/L NOEC > 180 mg/L LOEC > 180 mg/L
4.3	Toxicity to Aquatic Plants e.g. *Algae*	*Selenastrum Capricornutum* ATCC22662	OECD TG 201	EC_{50} (72 hr) > 100mg/L NOEC(72 hr) > 100mg/L
4.5.1	Chronic Toxicity to Fish			None

4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 211	NOEC(21d,reproduction)= 55.6 mg LOEC(21d,reproduction)>100mg/L EC_{50}(21d, reproduction) >89.1mg/L LC_{50} for parental *Daphnia*(21d)>100 mg/L NOEC=0.0082 (21d, reproduction, parent *Daphnia* mortality)
4.6.1	Toxicity to Soil Dwelling Organisms			None
4.6.2	Toxicity to Terrestrial Plants			None
4.6.3	Toxicity to Other Non- Mammalian Terrestrial Species (Including Birds)			None
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD_{50} > 2,000 mg/kg (for both sexes)
5.1.2	Acute Inhalation Toxicity	Rat	Other	2,600 mg/m^3 (4hr)
5.1.3	Acute Dermal Toxicity	Rabbit	Other	LD_0 > 2.0 mL/kg
5.2.1	Skin Irritation	Rabbit	Other	Slightly irritating
5.2.2	Eye Irritation	Rabbit	Other	Slightly irritating
5.3	Skin Sensitisation	Guinea pig	OECD TG 406	Not sensitizing
5.4	Repeated Dose Toxicity	Rat	OECD TG 421	NOAEL = 100 mg/kg bw LOAEL = 300 mg/kg bw
5.5	Genetic Toxicity *In Vitro*			
A.	Bacterial Test	*S.typhimurium*, *E. coli*	Japanese Guideline and OECD TG 471 & 472	- (With metabolic activation) - (Without metabolic activation)
B.	Non-Bacterial *In Vitro* Test	CHL/IU cells	Japanese Guideline	- (With metabolic activation) - (Without metabolic activation)
5.6	Genetic Toxicity *In Vivo*	Mouse	Other	No valid data
5.7	Carcinogenicity	Mouse	Other	No valid data
5.8	Toxicity to Reproduction	Rat	OECD TG 421 Preliminary toxicity screening test	NOAEL = 100 mg/L (male) NOAEL = 1,000 mg/L (female) NOAEL = 1,000 mg/L (Offspring)
5.9	Developmental Toxicity/ Teratogenicity			None
5.11	Experience with Human Exposure			None

[Note] Data beyond SIDS requirements can be added if the items are relevant to the assessment of the chemical, e.g. corrosiveness/irritation,carcinogenicity.

SIDS Initial Assessment Report
for
13th SIAM
(November 6-9, 2001)

Chemical Name: Tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate

CAS No: 3319-31-1

Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:
Mr. Koji Tomita, Ministry of Foreign Affairs, Japan

HISTORY:
The original IUCLID documents were prepared by European Commission. Dainippon Ink and Chemicals Inc., Japan reviewed the documents after incorporation of Japanese testing results.

COMMENTS:
ICCA Initiative work led by Dainippon Ink and Chemicals Inc., Japan

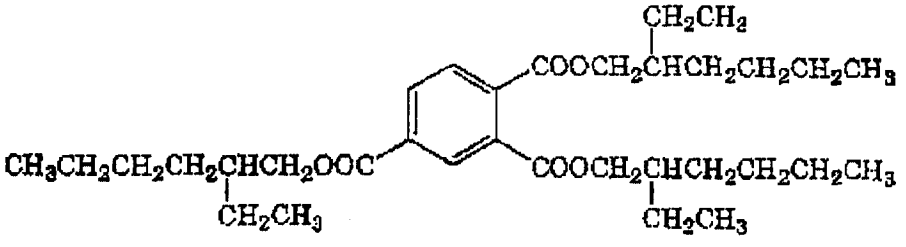
Deadline for circulation:
Date of Circulation:

SIDS INITIAL ASSESSMENT REPORT (SIAR)

Tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate

1. IDENTITY

IUPAC Name: Tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate
CAS Number: 3319-31-1
Molecular formula: $C_{33}H_{54}O_6$ (MW=546.79)
Structural formula:



Synonym: TOTM
Tris(2-ethylhexyl) trimellitate
Benzene-1, 2, 4-tricarboxylic acid tris-(2-ethylhexyl) ester

Purity: >99.5%

Impurity: Di(2-ethylhexyl) phthalate (DEHP) < 0.1%
Water

Additives: None

Table 1. Physical and Chemical Properties

Items	Protocol	Results
Melting Point	OECD TG 102	< -50°C
Boiling Point	Unknown	283°C(4 hPa)
Density	Unknown	0.987 - 0.990 g/cm³(20°C)
Vapor pressure	OECD TG 104	<2.8 x 10^{-4} Pa(100°C)
Partition Coefficient (LogP_{ow})	OECD TG 107	5.94 (25°C)
Water Solubility	OECD TG 105	0.13 mg/ L (25°C)

2. GENERAL INFORMATION ON EXPOSURE

The production volume of TOTM in Japan is approximately 20,000 tonnes /year and also, there are 5 manufacturers in Japan. Estimated global production is 40,000 – 100,000 tonnes/year. TOTM is produced in closed system and mainly used as plasticizer for PVC electrical cable and wire especially for high temperature application. TOTM is no source of potential release to the environment except for sampling and maintenance of the production facilities.

2.1 Environmental Fate

Based upon the biodegradation measurement, the substance is not readily biodegradable. TOTM achieved 4.2 percent of its theoretical BOD using an activated sludge inoculum during a 4 weeks incubation in a single screening study.

The Mackay levelIII fugacity model was employed to estimate the environmental distribution of TOTM in air, water, soil and sediment. The calculation results are shown in Table 2.If released to air, an estimated vapor pressure of less than 2.8 x 10^{-4} Pa at 100°C indicates TOTM will exist solely in the particulate-phase in the ambient atmosphere. Particulate-phase TOTM is removed from the atmosphere by wet and dry deposition. If released to soil, TOTM isnot expected to have mobility based upon the fugacity model calculation Volatilization from soil surfaces is not expected to be an important environmental fate process based on theestimated vapor pressure of this substance. If released into water, TOTM is expected to adsorb to suspended solids and sediment in water based upon thefugacity model calculation. [Dainippon Ink and Chemicals, Inc. (2001)]
Hydrolysis may be an important environmental fate process based onestimated hydrolysis half-lives of 17.5 and 11.9 days at pH 7 and 9, respectively. Measured BCF values of less than1 to 2.7 in carp suggest that bioconcentration in aquatic organisms is low.

Table 2. Predicted distribution of TOTM using Fugacity level III (%)

Compartment	*Release 100% to air*	*Release 100% to water*	*Release 100% to soil*
Air	19.6	0.0	0.0
Water	4.7	32.7	0.0
Soil	66.2	0.1	100.0
Sediment	9.5	67.2	0.0

2.2 Human Exposure

2.2.1 Occupational exposure

The substance is produced and used in closed system. So, occupational exposure is limited in the case of sampling and maintenance at the production facilities. Moreover, the exposure time is very short. The major rout of occupational exposure is inhalation and dermal.
The atmospheric concentration was measured at two production sites in Japan. The monitoring data are shown in Table 3. The maximum exposure level is estimated according to working schedules as follows. From Table 3, if a single worker (Body weight; 70 kg, respiratory volume; 1.25 m^3/hour) is assigned to implement all daily operation without protection, the daily intake (EHE inh) is calculated as 1.77 x 10^{-3} mg/kg/day as the worst case. On the other hand, a single worker (surface area of exposed skin 840 cm^2 for hands) daily dermal dose (EHE der) is calculated as 2.47 mg/kg/day based on below calculation as the worst case without protection. Workers wear protective gloves and goggles during the operation, so significant exposure is not expected.

Table 3. Available workplace monitoring data for TOTM (EHE inh)

Occupation	Frequency Times/day	Duration Hr	Working hr/day	Max concentration mg/m^3	EHE inh mg/kg/day	Reference
Sampling	5	0.017	0.085	0.210	3.19x10^{-4}	JISHA, Japan (2001)
Analysis	5	0.067	0.335	0.053	3.17x10^{-4}	
Charge to drum	1	0.833	0.833	0.076	1.13x10^{-3}	
Total	11	-	1.253	-	1.77x10^{-3}	

EHE inh: Estimated Human Exposure for inhalation

Calculation: EHE der = (Cder * T * S * t) /W

EHE der: Estimated Human Exposure for dermal
Cder = 990 mg/cm^3 (Rate in product contacted by worker)
T = 0.01 cm (Thickness of substance)
S = 840 cm^2 (Surface area of exposed skin) for hand
t = 0.0208 day/day (Exposure time per day ; 10min/8Hr, [1day = 8Hr] assumed)
W = 70 Kg (body weight)

2.2.2 Consumer exposure

Usually, this substance has been already blended to the compound asplasticizer, so it is not expected that downstream users or consumers of electric wire industry may expose to this substance.

3.HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics and metabolism

Absorption and metabolism were studied for TOTM(14C-labeled on the 2-carbon atom of 2-ethylhexyl group) mixed with corn oil and administered by gavage in a single dose of 100 mg/kg of body weight in 4 male SDrats. About 75% of the dosewas excreted unchanged in the feces, 16% in the urine as metabolites and 1.9% was expired as $^{14}CO_2$. Radioactivity was excreted in the feces as unchanged TOTM (85% of the fecal radioactivity), mono- and di(2-ethylhexyl)trimellitate(MOTM and DOTM, respectively), and as unidentified polar metabolites. Metabolites in the urine were identified as MOTM and metabolites of 2-ethylhexanol less than 0.6% of the dose remained in the tissues. Elimination of $^{14}CO_2$ was biphasic with half-lives of 4.3 and 31 hrs, and excretion of radioactivity in the urinewas biphasic with half-lives of 3.4 hrs and 42 hrs. [Eastman Kodak Company]

3.1.2 Acute toxicity

Acute toxicity data are mainly reported for rat, mice and rabbits. We could find 12 acute toxicity data for animals(oral(6), inhalation(1), IP(2) and dermal(3)) test data, and one(oral) study (MHW, Japan (1996)) and two(oral and dermal) studies (Nuodex Inc.(1981), Nuodex Inc(1982c)) were conducted by the method of OECD TG and similar method to OECD TG, respectively.
The data, which we feel informative to evaluate the acute toxicity, are listed in Table 4.

Table 4. Summary of effects of TOTM on animals (Acute Toxicity)

Route	Animals	Values	Type	References
Oral	Rat	>2000 mg/kg	LD_{50}	MHW, Japan (1996)
	Rat	>5000 mg/kg bw	LD_0	Nuodex Inc.(1981)
Inhalation	Rat	>2600 mg/m^3	LC_0	Nuodex Inc.(1982b)
Dermal	Rabbit	>2 ml/kg	LD_0	Nuodex Inc(1982c)
	Rabbit	>1970 mg/kg bw	LD_0	Tenneco Chemicals(1981))
I.P.	Rat	>3200 mg/kg bw	LD_{50}	Eastman Kodak (1983)
	Mouse	>3200 mg/kg bw	LD_{50}	Eastman Kodak (1983)

It can be concluded that acute toxicity (Oral) of TOTM is LD_{50} >2000 mg/kg in rat.

3.1.3 Repeated dose toxicity

Among the eight available data, four were conducted under the GLP. Three studies were considered to be key study.

The first study was the oral study by CMA(1985). The subchronic toxicity of TOTM administered orally in the diet togroups of 5 male and 5 femaleFischer 344 rats at levels of 0(0), 0.2(184), 0.67(650), 2.0(1826) % (mg/kg bw/day) for 28 days was detemined. There were no statistically significant differences in body weights between control andTOTM treated groups. There was a significant difference between control and treated groups in thefollowing: absolute and relative liver weights (higher in both sexes at all levels except 0 or 0.2%)serum albumin (higher in both sexes at 0.67 or 2.0%), serum cholesterol levels (higher in males at 0.67 or 2.0%). Liver biochemistry revealed statistically significant differences between treated and control groups as indicated by palmitoyl CoA oxidation (increased in both sexes at 20% and males at all dose levels), andcatalase activity (increased inmales at 2.0%). So, the NOAEL for repeated dose toxicity is considered to be 184 mg/kg and the LOAELis 650 mg/kg for both sexes.

The second study was the oral study by MHWJapan(1996). No test substances related changes were noted in terms of clinical signs, body weight, food consumption, and hematology, blood examination, urinalysis, and pathological findings. So, the NOEL for repeat dose toxicity is considered to be 1,000 mg/kg/day for both sexes.

The third study was the OECD preliminary reproduction toxicity screening test by MHW Japan(1998). Gavage study in SD rats conducted at doses of 100, 300 and 1,000 mg/kg/day (Male; 46days, Female; from 14days before mating to day 3 of lactation)of TOTM. The decreases in spermatocytes and spermatids in males was observed for 300 and 1,000 mg/kg groups by histopathological examination. No effects on general appearance, body weight, food consumption, autopsy findings, weights of the reproductive organs ofboth sexes, or histopathlogical features of the ovary were detected. So, the NAOEL is considered to be 100 mg/kg/day for males, and 1,000 mg/kg/day for females.

There is no available information on human toxicity.

Conclusions:

The NOAEL and the LOAEL for repeated oral toxicity are considered to be 100 and 300 mg/kg/day for rats, respectively.

3.1.4 Genotoxicity / Mutagenicity

We can find five reports for Ames Tests. One (MHW, Japan: 1996) is conducted under GLP and others are not. The study of MHW is considered to be a key study.
TOTM has been investigated *in vitro* tests. This substance did not induce gene mutation in bacterial system (MHW, Japan: 1996), and chromosomal aberration in mammaliancultured cells (MHW, Japan: 1996), with and without an exogenous metabolic activation system. Among these studies, MHW study was identified to be a key study because it was well conductedand reported.

Reverse gene mutation assay was conducted by OECD TG 471and 472, using pre-incubation method. TOTM was not mutagenic in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and Escherichia coli WP2 uvrA at concentration of up to 5000 ug /plate, with or without an exogenous metabolic activation system (MHW, Japan: 1996).

Chromosomal aberration test by OECD TG 473 was conducted in cultured Chinese hamster lung (CHL/IU) cells. Structural chromosomal aberrations and polyploidy were not inducedup to a maximum concentration of 5.0 mg/mL on continuous treatment, and with Short-term treatment, with and without an exogenous metabolic activatio system (MHW, Japan: 1996).

And all other test results (HGPRT assay, Unscheduled DNA synthesis, Dominant Lethal Assay for example) shows that TOTM is not genetoxic

Conclusions:
This substance is considered to be not genotoxic with and without an exogenous metabolic activation system in bacterial test and chromosomal aberration test*in vitro*.

3.1.5 Carcinogenecity

One brief report states only that tests in mice, with a propensity to form pulmonary adenomas, were negative for TOTM, unlike those using urethane. Thecarcinogenecity tests revealed that the chemical is negative but test result was invalid.

3.1.6 Reproduction/developmental toxicity

The OECD Preliminary Reproduction Toxicity Screening Test was performed. [MHW, Japan: 1998]. This study was identified to be well conducted andreported.
Gavage study in SD rats conducted at doses of 100, 300 and 1,000 mg/kg/day (Male; 46days, Female; from 14days before mating to day 3 of lactation)of TOTM.
Histopathological examination of the testes revealed decreases inspermatocytes and spermatids in males of the 300 and 1,000 mg/kg groups. No effects of TOTM were detected on general appearance, body weight, food consumption, autopsy findings, and weight of reproductive organs of both sexes, or on histopathological examination of the ovary. On the basis of these findings, the NOELs of TOTM for repeat dose toxicity are considered to be 100 mg/kg/day for males, and 1,000 mg/kg/day for females.
Except for the effects in males observed on histopathological examination, no influence of this substance was detected regarding reproductive ability, organ weights or histopathological appearance of the ovaries, delivery or maternal behaviorof dams. No effect of TOTM were detected on viability, general appearance,body weight or autopsy findings of offspring.On the basis of these findings, theNOELs for reproductive/ developmental toxicitywere considered to be 100mg/kg/day for male rats, 1,000 mg/kg/day for female rats, and 1,000 mg/kg/day for offspring.

Conclusions:

The NOELs for reproductive/developmental toxicity were considered to be 100 mg/kg/day for male rats, 1,000 mg/kg/day for female rats, and 1,000 mg/kg/day for offspring, respectively.

3.1.8 Other : Irritation and sensitization

Six and three results are reported for skin and eye irritation test, respectively. All these test results showed that TOTM is slightly irritating to the skin and the eye.

Sensitization test on guinea pig using OECD/TG 406 (Tenneco Chemicals, 1981) showed " no sensitization".

3.2 Initial Assessment for Human Health

Acute toxicity of TOTM is considered to be LD_{50} >2000 mg/kg in rat.
In the irritation-test for animals, TOTM is slightly irritating to the skin and the eye.
Sensitization test on guinea pig using OECD/TG 406 showed " no sensitization".
The NOAEL and the LOAEL for repeated oral toxicity are considered to be 100 and 300 mg/kg/day for rats, respectively
The NOELs for reproductive/developmental toxicity were considered to be 100 mg/kg/day for male rats, 1,000 mg/kg/day for female rats, and 1,000 mg/kg/day for offspring, respectively.
This substance is not genotoxic with and without an exogenous metabolic activation system in bacterial test and chromosomal aberration test *in vitro*.

TOTM produces the same spectrum of morphological and biochemical change in the rat liver as DEHP. TOTM, however, was much less potent in its action, with a dietary level of 2.0%, causing less peroxisome proliferation and peroxisome-associated enzyme induction than 0.67% DEHP. Also, the level of peroxisome induction in rats given TOTM is less than in those receiving a metabolically equivalent dose of 2-ethylhexanol. Furthermore, on a molar basis, effects were lower than with DEHP. An effect of MEHP, a metabolite of DEHP, was not seen with TOTM. [The British Industrial biological Research Association (1985), EPA OTS0510637(1985), JOHN R. HODGSON. (1987)]

In addition, recently studies have determined that rodents (rats) are susceptible to peroxisome proliferation. After all, these results suggest that the effect of DEHP on liver are markedly different between other species (marmosets) and rodents (rats). Yoshimasa Kurata et al. (1998)] Therefore, DEHP was downgraded from Group 2B to Group 3 by the IARC Monographs Working Group. (February 2000) Group 3 is " cannot be classified as to its carcinogenicity to humans".

4. Hazards to the Environment

4.1 Aquatic Effects

TOTM has to be considered as weakly toxic against aquatic organisms. Aquatic effects were tested and results are summarized in Table5. As the lowest acute and chronic toxicity data, EC_{50} (>100 mg/L ,72hr) of *Selenastrum capricornutum* ATCC22662 and NOEC (55.6 mg/L, 21day) of Daphnia magna were adopted, respectively.

Table 5. Summary of effects of TOTM on aquatic organisms

Organism	Test duration	Result (mg/L)	Reference
Algae			
Selenastrum capricornutum ATCC22662	72 hr	EC_{50} >100 NOEC>100	EA, Japan
Invertebrates			
Daphnia magna	24 hr	EC_{50} >180	EA, Japan
	48 hr	EC_{50} >180 NOEC>180	
	48hr	EC_{50} >1	ICI 1990
	21 day	EC_{50} =89.1 NOEC=55.6	EA, Japan

	21day	NOEC=0.082	CMA (1985)
Fish			
Oryzias latipes	96 hr	LC_{50} >100	EA, Japan
	14 day	LC_{50} >75 NOEC>75	EA, Japan

As the acute toxicity data, EC_{50} (>100 mg/L ,72hr) of *Selenastrum capricornutum* ATCC22662 and EC_{50} (180 mg/L, 48hr) of Daphnia magna were adopted, respectively. As the chronic toxicity data of Daphnia magna and the prolonged toxicity data of fish (Oryzias latipes), NOEC =0.082mg/L (21days) [CMA; 1985] and NOEC=75mg/L (14days) [EA Japan] were adopted, respectively. All those data in supersaturated solution, which was considered to be homogeneous substantially, was obtained with the aid of solubilizer (HCO-40). Though the observed concentration data was less reliable, one chronic toxicity data (NOEC >0.082mg/L) was reported in a lower concentration than saturation point.

Two other acute (ICI 1990) and chronic(EA Japan) data would be helpful for evaluation of the toxicity for Daphnia magna. These tests were conducted in a supersaturated solution.

Assessment factor of 100 was chosen to determine the lowest PNEC. Thus, calculated PNEC (=0.00082 mg/L) of TOTM is closely to the value of one hundredths (assessment factor) of saturation point. From these toxicity data, it is difficult to decide the exact PNEC, but we are sure that TOTM is practically non-toxic against aquatic organisms.

4.2 Terrestrial effects

There is no available information.

4.3 Initial assessment for the Environment

Hydrolysis may be an important environmental fate process based onestimated hydrolysis half-lives of 17.5 and 11.9 days at pH 7 and 9, respectively. The substance is not readily biodegradable. Measured BCF values of this chemical is reported asless than 1 to 2.7 in carp for 6 weeks, which suggest that bioconcentration in aquatic organisms is much lower than the value estimated from logPow(=5.94). If released into surface water water, TOTM is expected to adsorb to suspended solids and sediment based upon the fugacity model calculation. The sediment toxicity data was not available, and will need to assess when obtained.

5. Conclusions and recommendations

5.1 Conclusions

Exposure (Physical/chemical property, production, use and distribution)
TOTM is manufactured as the plasticizer of PVC application.
The production volume of TOTM in Japan isapproximately 20,000 tonnes /year and also, there are 5 manufacturers in Japan. Estimated global production is 40,000 – 100,000 tonnes/year. TOTM is produced in closed system andmainly used as plasticizer for PVC electrical cable and wire. And so, this substance has been already blended to the compound aplasticizer, so it is not expected that downstream users or consumers of electric wire industry may expose to this substance.

Occupational exposure may occur through dermal contact and inhalation of vapor. The process

is constructed by closed system and workers wear protective gloves and gggles during the operation, so significant exposure is not expected.
In case of disposal, this substance would be incinerated with following all regulations. Therefore, it is not significant released to theenvironment

Human health
Acute toxicity of TOTM is low, LD_{50} >2,000 mg/kg in rats. In the irritation-test for animals, this substance is slightly irritating to the skin and the eyes. Sensitization test on guinea pig showed "no sensitization". Oral study in rats conducted for 28 days at doses of0(0), 0.2(184), 0.67(650), 2.0(1826) % (mg/kg bw/day) of TOTM. There were no statistically significant differences in body weights between control andTOTM treated groups. There was a significant difference between control and treated groups in thefollowing: hemoglobin concentration (lower in both sexes, 0.67 or 2.0% TOTM), leucocyte counts (higher in males at 0.67 or 2.0%), absolute and relative liver weights (higher in both sexes at all levels except 0 or 0.2%),serum albumin (higher in both sexes at 0.67 or 2.0%), serum cholesterol levels (higher in males at 0.67 or 2.0%), serum urea (higher in males at 2.0%), serum lipids (decreased in females at0.2%). Liver biochemistry revealed statistically significant differences between treated and control groupsas indicated by palmitoyl CoA oxidation (increased in both sexes at 20% and males at all dose levels), and catalase activity (increased in males at 2.0%). Therefore, the NOAEL and the LOAEL for repeated oral toxicity were considered to be100 and 300 mg/kg/day for male rats.
The NOELs for reproductive/developmental toxicity were considered to be>1,000 mg/kg/day for female rats and for offspring.
TOTM is not genetoxic/mutagenic in bacterial and mammalian cell tests*in vitro* tests. The carcinogenecity tests revealed that the chemical is negative but test result was invalid.

Environment
The Mackay levelIII fugacity model was employed to estimate the environmental distribution of TOTM in air, water, soil and sediment. If released to air, TOTM will exist solely in the particulate-phase in the ambient atmosphere. If released to soil, TOTM is not expected to have mobility. If released into water, TOTM is expected to adsorb tosuspended solids and sediment in water.
Measured BCF of values of less than 1 to 2.7 in carp suggest that bioconcentration in aquatic organisms is low.

As the lowest acute and chronic toxicity data, EC_{50} (>100 mg/L, 72hr) of *Seletiastrum capricornutum* ATCC22662 and NOEC (0.082mg/L, 21day) of Daphnia magna were adopted, respectively. Assessment factor of 100 was chosen to both acute and chronic toxicity data to determine PNEC Thus, PNEC of TOTM is 0.00082mg/L.

5.2 Recommendations
The chemical is currently of low priority for further work.

6. References
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Midwest Research Institute; Thomas W. Lapp, Charles E Mumma Joseph Chaszar: A Survey of Plasticizers : Epoxies, Linear Polyesters and Trimellitates Chemical Technology and Economics in Environmental Perspective, Task IV, Environmental Protection Agency (Nov. 1981)

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Nuodex Inc. Acute oral toxicity– Rats Doc ID878214469 (1981)

The British Industrial biological Research Association; A 28-day Toxicity Study with TOTM in the Rat with Cover Letter Dated 111885. (1985)

Yoshimasa Kurata. Subchronic Toxicity of Di(2-ethylhexyl)phthalate in Common Marmosets: Lack of Hepatic Peroxisome Proliferation, Testicular Atrophy, or Pancreatic Acinar Cell Hyperplasia. Toxicological Sciences 42, 49-56 (1998)

PROPOSED ROBUST SUMMARY for Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate

CAS No. 3319-31-1

Sponsor Country: Japan

Date: Aug 24, 2001

PHYSICAL/CHEMICAL ELEMENTS

MELTING POINT

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 102
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** Not stated.

RESULTS

- **Melting point value:** <-50 °C (223 K)
- **Decomposition:** Not stated.
- **Sublimation:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Melting point is <-50°C (223 K).

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BOILING POINT (a)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Boiling point value:** 283°C
- **Pressure:** 4
- **Pressure unit:** hPa
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Boiling point is283°C at 4 hPa.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES

Midwest Research Institute; Thomas W. Lapp, Charles EMumma Joseph Chaszar: A Survey of Plasticizers: Epoxies, Linear Polyesters andTrimellitates Chemical Technology and Economics in EnvironmentalPerspective, Task IV, Environmental Protection Agency (Nov. 1981)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BOILING POINT (b)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Boiling point value:** 414°C (687K)
- **Pressure:** 1,013
- **Pressure unit:** hPa
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Boiling point is414°C at 1,013hPa.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** The Sigma-Aldrich Library of Regulatory and Safety Data.

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

DENSITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Density:** 0.987 – 0.990 g/cm^3
- **Temperature:** 20°C
- **Remarks:** Not stated.

CONCLUSIONS

Density is 0.987-0.990 g/cm^3 at 20°C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES

Midwest Research Institute; Thomas W. Lapp, Charles E Mumma Joseph Chaszar: A Survey of Plasticizers: Epoxies, Linear Polyesters and Trimellitates Chemical Technology and Economics in Environmental Perspective, Task IV, Environmental Protection Agency (Nov. 1981)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

VAPOR PRESSURE (a)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 104
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** Not stated.

RESULTS

- **Vapour Pressure value:** $< 2.8 \times 10^{-4}$ Pa
- **Temperature:** 100 °C
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Vapour pressure is $< 2.8 \times 10^{-4}$ Pa at 100 °C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

VAPOR PRESSURE (b)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method/guideline:** Not stated
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:** Not stated.

RESULTS

- **Vapour Pressurevalue:** 0.27 – 6.7 hPa
- **Temperature:** 250 – 260 °C
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Vapour pressure is 0.27- 6.7 hPa at 250 – 260 °C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES

Midwest Research Institute; Thomas W. Lapp, Charles EMumma Joseph Chaszar: A Survey of Plasticizers: Epoxies, Linear Polyesters andTrimellitates Chemical Technology and Economics in Environmental Perspective, Task IV, Environmental Protection Agency (Nov. 1981)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

PARTITION COEFFICIENT

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene 1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 107 (Shake Flask Method, 1995)
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** Not stated.

RESULTS

- **Log P_{ow} :** 5.94
- **Temperature:** 25°C ±1°C
- **Remarks:** Test condition: Test was conducted in duplicate under the following three conditions. Test chemical was analyzedby HPLC.

Test condition	Condition-1	Condition-2	Condition-3
1-Octanol saturated with water	10 mL	20 mL	40 mL
Water saturated with 1-octanol	240 mL	230 mL	210 mL
Test chemical in 1-octanol saturated with water (52.2 mg)	10 mL	10 mL	10 mL

Test results	Log Pow		
	a	b	Mean
Condition-1	5.99	5.99	
Condition-2	5.95	5.87	5.94
Condition-3	5.92	5.93	

CONCLUSIONS log P_{ow} is 5.94.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**

Remarks:

WATER SOLUBILITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method:** OECD TG 105 (flask method).
- **GLP:** Yes
- **Year:** 1998.
- **Remarks:** Not stated.

RESULTS

- **Value:** 0.13 mg/L at 25 °C±1°C
- **Description of solubility:** Of very low solubility
- **pH value:** No dissociation group.
- **pKa value:** There is no pertinent functional group.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is very low solubility in water.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- Order number for sorting
- **Remarks:**

ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS

STABILITY IN WATER

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 111
- **Type :** Hydrolysis as a function of pH
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** No hydrolysis of test chemical was observed at pH 4 at 50°C±1°C for 5 days. Hydrolysis rates at pH 7 were determined at 60, 70 and 80 °C, and at pH 9 at 50, 60, and 70 °C . They were extrapolated to 25 °C using Arrhenius relationship. Half life at 25 °C was calculated from the rate constant.

RESULTS

- **Nominal:** ca. 0.2 mg/L
- **Measured value:** Not stated.
- **Degradation:** No hydrolysis occurred in 5 days, at 50 °C pH 4. At pH 7 and pH 9, test chemicals were hydrolysed at all temperatures studied.
- **Half-life ($t_{1/2}$):**

	Rate Constant (hr^{-1})	Half-life(day)
pH 7	1.65×10^{-3}	17.5
pH 9	2.44×10^{-3}	11.9

- **Breakdown products:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is stable in aqueous water at pH 4 under the condition studied, but it ishydrolysed at pH 7 and pH 9 at 25 °C with half-life of 17.5 and 11.9 days.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Not applicable.

METHOD

- **Test:** Calculation
- **Method:** Fugacity level III
- **Year:** 2001
- **Remarks:** The parameters used are shown in Appendix.

RESULTS

- **Media :**
- **Estimated Distribution under three emissionscenarios:**

Compartment	Release100 % to air	Release 100 % to water	Release 100 % to soil
Air	19.6 %	0.0 %	0.0 %
Water	4.7 %	32.7 %	0.0 %
Soil	66.2 %	0.1 %	100.0 %
Sediment	9.5 %	67.2 %	0.0 %

- **Remarks:**

CONCLUSIONS

If this chemical is released into water the majority of this chemical is expected to stay in sediment, but if it is released into air or soil, this chemical is expected to stay in soil

DATA QUALITY

- **Reliabilities:** Key study.
- **Remarks:** Not stated.

REFERENCES

Dainippon Ink and Chemicals, Incorporated (2001), unpublished report.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BIODEGRADATION

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Unavailable

METHOD

• **Method:**	OECD TG 302C "Inherent Biodegradability: Modified MITITest(II)"
• **Test Type:**	Aerobic
• **GLP:**	No
• **Year:**	1977
• **Contact time:**	28 days
• **Inoculum:**	The supernatant (500ml) of activated sewage sludge obtained fromten sampling sites and 5 liters of supernatant removed from a previously established culture are transferred to a culture vessel. The pH of the culture mixture was adjusted to 7.0±1.0 and constantly aerated . Thirty minutes after stopping aeration, discard about 1/3 of the whole volume of the supernatant, and add an equal volume of 0.1% synthetic sewage and the aeration re-started. Repeat this procedure once a day.
• **Remarks:**	During the aeration, appearance of supernatant and the formation of activated sewage was observed. The sludge was found to form a clear supernatant on settling and formed cloudyflocs when on aeration. Operating temperature, pH and a dissolved oxygen concentration were recorded. The protozoa of sludge were observed under an optical microscope. *Incubation apparatus: Respirometry(Closed bottle) Ohkura Electric Co. *CO2 absorbent: Soda lime No.1 (Wako pure chemicals Inc.) *Stirrer : Magnetic stirrer *Temperature : 25±1℃ *Concentration of test chemical: 30mg/L, 100mg/L *Reference substance: Aniline

RESULTS

• **Degradation:**	
• **Results:**	4.2% after 28days
• **Kinetic:**	The percentage degradation in term of oxygen consumption was calculated as follows: % degradation = (BOD-B)/TOD x 100 BOD: Biological Oxygen Demand of the test material B : Oxygen consumption in basal culture medium to which inoculum is added (control) TOD: Theoretical oxygen demand to completely oxidize the test Material
• **Breakdown products:**	Not stated.

- **Remarks:** At the end of incubation, measure the residual dissolved organic carbon and test material concentration. The reference substance, aniline, attained more than 40% and 60% degradation after 7 and 14days confirming the suitability of the inoculum and culture conditions.

CONCLUSIONS

This chemical is low biodegradable.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemical Inspection and Testing Institute.

REFERENCES

Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan(1992)

Ministry of International Trade and Industry

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BIOACCUMULATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable

METHOD

- **Method:** OECD TG 305C
- **Species:** *Cyprinus Carpio* (Obtained from Nakajima hatchery in Kumamoto, Japan)
- **GLP:** No
- **Year:** 1978
- **Exposure Period:** 42 days
- **Remarks:**

Test fish: Acclimated for ca. 8 weeksbefore testing at 25±2°C. Fish with ca.10cm In length and ca.30g in weight were selected at random. Lipid content was 2-6%.

Test condition: Concentrations: 0.2 and 2 mg/L, solubilizer controlled
Type of test: flow-through (200-800mL/min), 100L glass tank.
Dissolved oxygen concentration: 6-8mg/L
Temperature: 25 ±2°C
Water chemistry was tested in the control and two concentrations every 2 times in a week.
Test was conducted in duplicate every 2 weeks for two concentrations (The control was done before and after testing.)

RESULTS

- **Results:** BCF=1-2.7 (concentration: 0.2mg/L)
  BCF=0.1-0.23(concentration: 2mg/L)
- **Kinetic:** BCF=C1/C2
  C1: Concentration of this chemical in Fish
  C2: Concentration of this chemical in water
- **Breakdown products:** Not stated.

CONCLUSIONS

This chemical is low bioaccumulation.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out byChemical Inspection and Testing Institute

REFERENCES

Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan(1992)

Ministry of International Trade and Industry

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

ECOTOXICITY ELEMENTS

ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method:** OECD TG 203
- **Type:** Semi-static
- **GLP:** Yes
- **Year:** 1998.
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka): Obtained from commercial domestic
- hatcheries.
- **Analytical monitoring** Yes. Test solutions were measured byHPLC before and after 24 hours exposure period. Test solutions were replaced every 24 hours to new ones.
- **Exposure period (h):** 96
- **Statistical methods:** Not applicable because of no mortality.
- **Remarks:**

Test fish: Acclimated for more than 12 days before testing; any groups showing no mortality for 7 days before test started. Fish with 22.1 mm (18.3–23.8 mm) in length were selected at random. Average body weight of fishwas 0.1462g (n=10).

Test conditions: Details of test: Semi-static (water changedevery 24 hours)
Dilution water source: Tap water after dechlorinated by passing through activated carbon.
Dilution water chemistry: Hardness: 25 mg/L as $CaCO_3$; pH: 6.7
Stock and test solution and how they are prepared: Pipette or pour the appropriate amount of the solution (0.3 wt% of test chemical)with solubilizer hydrogenated caster oil HCO-40 3000mg/l) into the test waters.
Concentrations dosing rate, flow-through rate, in what medium: Concentrations of 0, 100 mg/L and dispersant control weretested.
Vehicle/solvent and concentrations: Hydrogenated caster oil HCO-40, 100mg/L
Stability of the test chemical solutions: Stable, measured concentration was 101-103%.
Exposure vessel type: 10 fish per group in 3L glass beaker without acration under room light
Number of replicates, fish per replicate: One replicatewas done.
Water chemistry in test (O_2, pH) in the control and all concentration where effects were observed: Dissolved oxygen readings and pH values were taken daily during 96 h exposure period.
Dissolved oxygen concentration: 5.0–9.2 mg/L.

pH values: 6.7~6.8.
Test temperature range:Water temperature at 23.5~24.1°C.
Method of calculating mean measured concentrations: Geometric mean.

RESULTS

- **Nominal concentrations:** 0, 100 (mg/L)
- **Measured concentrations :** <1, 103 (0hr), <1, 102 (24hr)
- **Unit :** mg/L.
- **Element value** LC_{50} at 96 hours >100.0 mg/L based on nominal concentrations.
- **Statistical results as appropriate:**Not applied.
- **Remarks field for Results:**
  Biological observations Not described.
  Table showing cumulative mortality:

Percent mortality of *Oryzias latipes* exposed to the test chemical

Nominal concentration (mg/L)	Cumulative number of dead fish (% mortality)			
	24 hour	48 hour	72 hour	96 hour
Control	0(0)	0(0)	0(0)	1(10)
Dispersant Control	0(0)	0(0)	0(0)	0(0)
100	0(0)	1(10)	1(10)	1(10)

Lowest test substance concentration causing 100% mortality:
Not obtained under the test conditions studied.
Mortality of controls: 1 fish was dead at 96h.
Abnormal responses: At 24 hr, one fish showed abnormal breathing behaviour at 100mg/L.
Reference substances: Copper(II)sulfate pentahydrate. LC_{50} at 96h was 0.43 mg/L.
Any observations, such as precipitation that might cause a difference between measured and nominal values: It became clouded in 100mg/L concentration, but not precipitation.

CONCLUSIONS

LC50 (96h) > 100mg/L for fish.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
- Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**

- **Remarks field for GeneralRemarks:**

PROLONGED TOXICITY TO FISH

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kegyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method:** OECD TG 204
- **Type:** Flow-through.
- **GLP:** Yes.
- **Year :** 1998.
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka): Obtained from commercial domestic hatcheries.
- **Analytical monitoring:** Yes. Test solutions were measured byHPLC before and after 7, 14days exposure period.
- **Exposure period:** 14 day.
- **Statistical methods** Binomial method (TOXDAT MULTI-METHOD PROGRAM, USEPA)
  Dunnet method was used for LC_{50} and for fish body weight difference, respectively.
- **Remarks field for Test Conditions:**

Test fish: Acclimated for more than 12 days before testing; any groups showing≦9% mortality for 7 days before test started. Fish with 20.0 mm (18.5–21.6 mm) in length were selected at random. Average body weight of fish was 0.484g (0.1182–0.2014g)(n=10). Fish were starved for 24 hours before the test started.

Test conditions Details of test: Flow-through.
Dilution water source: Tap water after dechlorinated by passing through activated carbon.
Dilution water chemistry: Hardness: 15.3mg/L as $CaCO_3$; pH: 7.0
Stock and test solution and how they are prepared: The working solution (4.8wt% of test chemical with solibilizer HCO-40 controlled) was prepared with the dilution water. The test solution was supplied continuously by mixing the working solution and the dilution water with the help of a mechanically operated quantitative water-pump.
Concentrations dosing rate, flow-through rate, in what medium: Nominal concentrations of 0, 18.8, 37.5 and 75.0 mg/L and Dispersant control were tested.
Vehicle/solvent and concentrations:Hydrogenated caster oil HCO-40, Max. 75.0 mg/L
Stability of the test chemical solutions: It became clouded in high concentration, but not precipitation.
Exposure vessel type: 10 fish per group in 3L glass beaker without aeration under room light
Number of replicates, fish per replicate: One replicate was done.
Water chemistry in test (O_2, pH) in the control and one concentration where

effects were observed: Dissolved oxygen readings and pH values were taken every 3 days during the exposure period.
Dissolved oxygen concentration: 6.6~7.7 mg/L.
pH values: 6.9~7.2.

Test temperature range: Water temperature at 23.5~24.1°C (24±2°C).

Method of calculating mean measured:Geometric mean.

RESULTS

- **Nominal concentrations :**0, 18.8, 37.5, 75.0 (mg/L) and dispersant control
- **Measured concentrations :**

Measured concentration of the test chemical during a 14-day exposure of orange killifish (*Oryzias latipes*) under flow-through test conditions

Nominal concentration (mg/L)	Measured concentration (mg/L) (percent of nominal)			
	0 day	7 day	14 day	Mean
Control	<1.0	<1.0	<1.0	--
Dispersant Control	<1.0	<1.0	<1.0	--
18.8	17.7(94.1)	15.8(84.0)	15.5(82.4)	16.3(86.9)
37.5	35.7(95.2)	33.2(88.5)	30.0(80.0)	33.3(87.9)
75.0	70.6(94.1)	68.8(91.7)	71.2(94.9)	70.2(93.6)

- **Unit :** mg/L
- **Element value:**

LC_{50} (7 days) > 75.0mg/L (nominal concentration)
LC_{50} (14 days) > 75.0mg/L (nominal concentration)
NOEC (14 days) > 75.0 mg/L (nominal concentration)

- **Statistical results, as appropriate:**

The mean body weight of fish exposed toall concentration of the test chemical was not significantly different from controls during the test period(1fa=0.05, Dunnet).

- **Remarks field for Results:**

Biological observations: Not described.

Cumulative mortality:

Percent mortality of *Oryzias latipes* exposed to the test chemical under flow-through test Conditions

Nominal conc. (mg/L)	Cumulative number of dead fish (% mortality) (days)														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Control	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(10)	1(10)	1(10)
Disp. Cont.	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
18.8	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
37.5	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
75.0	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)

Fish weight:

Nominal conc. (mg/L)	Fish weight (g)										
	No.1	No.2	No. 3	No.4	No.5	No.6	No.7	No.8	No.9	No.10	Ave.
Control	0.1879	0.2526	0.1273	0.2239	0.1139	0.1434	0.1708	0.1789	0.1558	-a	0.1727
Disp. Cont.	0.2205	0.1827	0.1192	0.1884	0.1438	0.1823	0.1563	0.2120	0.1635	0.1580	0.1727
18.8	0.1731	0.1513	0.1593	0.1472	0.2150	0.1548	0.1547	0.1306	0.2104	0.1020	0.1598
37.5	0.1264	0.1495	0.1872	0.1237	0.2055	0.1396	0.1805	0.2101	0.1577	0.1303	0.1611
75.0	0.1746	0.1848	0.1804	0.1625	0.1494	0.1633	0.2103	0.1454	0.1600	0.1818	0.1713

- a : No measurement was made because the Orange Killifish was dead.

Lowest test substance concentration causing 100% mortality>75.0 mg/mL (nominal).

Mortality of controls:10 % mortality observed during the test period (12 through 14 days).
Food intake: Fish was fed with TetraMin® fish food (2% of fish body weight).
Abnormal responses: No abnormal response showed through 14 days.
Reference substances (if used)– results: Copper (II) sulfate pentahydrate. LC_{50} at 96h was 0.30 mg/L.
Any observations, such as precipitation that might cause a difference between measured and nominal values: It became clouded high concentration, butnot precipitation.

CONCLUSIONS

LC_{50} (7 days) > 75.0mg/L (nominal concentration)
LC_{50} (14 days) > 75.0mg/L (nominal concentration)
NOEC (14 days) > 75.0 mg/L (nominal concentration)

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed :**
- **Order number forsorting :**
- **Remark - field for GeneralRemarks :**

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (e.g., *Daphnia*)

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01 Purity: >95.0%

METHOD

• **Method:**	OECD TG 202
• **Type:**	Static
• **GLP :**	Yes
• **Year :**	1998
• **Species/Strain/Supplier:**	*Daphnia magna*
• **Analytical monitoring**	Yes. Test solutions were measured byHPLC before and after 48 hours exposure period.
• **Exposure period (h):**	48
• **Statistical methods:**	Not applicable.

Remarks field for TestConditions:

Test organisms:	Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan). Age at study initiation: Juveniles within 24h old. Control group: Yes.
Test conditions	Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1800mg/L(with solubilizer HCO-40 1000mg/L controlled) with diluting water (Elendt M4) before use.
Test temperature range:	19.9-20.2 °C (average temperature 20°C). Exposure vessel type: 100mL test solution in a 100 mL glass beaker; 4 beakers per treatment Dilution water source: Elendt M4(OECD guideline No.211 Annex 2) Dilution water chemistry: Hardness: 228mg/L as $CaCO_3$ Lighting: room light 16h:8h light-darkness cycle Water chemistry in test: DO= 8.0-8.6mg/L; pH=7.3-7.8. Feeding: none
Test design:	Number of replicates=20 Concentrations: 0, 17.1, 30.9, 55.6, 100 and 180 mg/L, because 48h-EiC_{50} for parent Daphnia (Acute immobilization test) was>1000mg/L. Dispersant control was also tested.
Method of calculating mean measured concentrations:	Geometric mean.
Exposure period:	48 h
Analytical monitoring:	By HPLC analysis. 95.1-99.6% of the nominal concentration at preparation; 90.1-97.7% after 48hr.

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (e.g., *Daphnia*)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method:** OECD TG 202
- **Type:** Static
- **GLP :** Yes
- **Year :** 1998
- **Species/Strain/Supplier:** *Daphnia magna*
- **Analytical monitoring** Yes. Test solutions were measured byHPLC before and after 48 hours exposure period.
- **Exposure period (h):** 48
- **Statistical methods:** Not applicable.

Remarks field for Test Conditions:

Test organisms: Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan).
Age at study initiation: Juveniles within 24h old.
Control group: Yes.

Test conditions: Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1800mg/L(with solubilizer HCO-40 1000mg/L controlled) with diluting water (Elendt M4) before use.

Test temperature range: 19.9-20.2 °C (average temperature 20°C).
Exposure vessel type: 100mL test solution in a 100 mL glass beaker; 4 beakers per treatment
Dilution water source: Elendt M4(OECD guideline No.211 Annex 2)
Dilution water chemistry: Hardness: 228mg/L as $CaCO_3$
Lighting: room light 16h:8h light-darkness cycle
Water chemistry in test: DO= 8.0-8.6mg/L; pH=7.3-7.8.
Feeding: none

Test design: Number of replicates=20
Concentrations: 0, 17.1, 30.9, 55.6, 100 and 180 mg/L, because 48h-EiC_{50} for parent Daphnia (Acute immobilization test) was>1000mg/L. Dispersant control was also tested.

Method of calculating mean measured concentrations:Geometric mean.

Exposure period: 48 h

Analytical monitoring: By HPLC analysis. 95.1-99.6% of the nominal concentration at preparation; 90.1-97.7% after 48hr.

RESULTS

- **Nominal concentrations:** 17.1, 30.9, 55.6, 100.0, 180.0 (mg/L) (Solubilizer controlled)
- **Measured concentrations :**

Measure Concentrations of test chemicals during a 48hr.

Nominal Concentration	Measured concentration(mg/L)			Percent of nominal	
(mg/L)	0hr	48hr	Mean	0hr	48hr
Control	< 1.0	< 1.0	-	-	-
Disp.Cont.	< 1.0	< 1.0	-	-	-
17.1	16.3	15.4	15.8	95.3	90.1
30.9	29.4	28.5	28.9	95.1	92.2
55.6	53.0	52.1	52.5	95.3	93.7
100.0	98.4	96.3	97.3	98.4	96.3
180.0	179.2	175.8	177.5	99.6	97.7

- **Unit :** mg/L.
- **Element value** EC_{50} at 24 hours >180.0 mg/L
  EC_{50} at 48 hours >180.0 mg/L
  NOEC > 180.0 mg/L
  LOEC > 180.0 mg/L
- **Statistical results as appropriate:** Not applied.
- **Remarks field for Results:**

Biological observations Not described.

Table showing mortality or immobility

Mortality or immobility of *Daphnia magna* to the test chemical

Nominal concentration (mg/L)	Cumulative number of dead or immobilized *Daphnia* (Percent Mortality or Immobility)	
	24 hour	48 hour
Control	0(0)	0(0)
Dispersant Control	0(0)	1(5)
17.1	0(0)	1(5)
30.9	0(0)	0(0)
55.6	0(0)	0(0)
100.0	0(0)	0(0)
180.0	0(0)	0(0)

Lowest test substance concentration causing 100% mortality:
Not obtained under the test conditions studied.

Mortality of controls: No mortality observed during test period.

Abnormal responses: No abnormal responses observed during test period

Reference substances: Potassium dichromate EC_{50} at 48h was 0.87 mg/L.

Any observations, such as precipitation that might cause a difference between measured and nominal values: It became clouded in high concentration, but not precipitation.

CONCLUSIONS

EC_{50} (48h) > 180mg/L and NOEC (48h) > 180mg/L for *Daphnia magna*.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed:**
- **Order number forsorting:**
- **Remarks field for GeneralRemarks:**

TOXICITY TO AQUATIC PLANTS (E.G., *ALGAE*)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method/guideline followed :** OECD TG 201
- **Test type :** Static.
- **GLP :** Yes
- **Year :** 1998
- **Species/strain # and source:** *Selenastrum capricornutum* ATCC22662 (purchased from ATCC)
- **Element basis:** Area under the growth curve.
- **Exposure period:** 72 h.
- **Analytical monitoring:** Yes, measured by HPLC at start and end of the test (72hr).
- **Statistical methods:** Bartlett test for homogeneity in variances and One-wayAnova (EcoTox-Statistics Ver.1.0 beta-edition R1.4) were used for EC_{50}, LC_{50} and NOEC determination (p=0.05).

Remarks field for Test Conditions :

Test organisms	Laboratory culture: OECD medium Method of cultivation: Shaking at 100rpm Controls: OECD medium. EC_{50} of potassium dichromate was 0.41 mg/L.
Test Conditions	Test temperature range: 23±2 °C Growth/test medium: OECD medium. Shaking: 100 rpm Dilution water source: OECD medium. Exposure vessel type: 100 mL OECD medium in a 300 mL Erlenmeyer flask with a silicon cap which allows ventilation. Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): pH=7.3-7.4 at start and 8.3-8.8 at end of the test (72 h). Stock solutions preparation: No stock solution was prepared. Test chemical was diluted to100mg/L (solubilizer, HCO-40 100mg/L)with OECD medium and sterilised with filter before use. Light levels and quality during exposure: 4,756-4,822 lux, continuous illumination.
Test design	Number of replicates: Triplicate Concentrations: 0, 100 mg/L and dispersant control were tested. Initial cell number in cells/mL: $1x10^4$

Method of calculating mean measured concentrations:Geometric mean.

RESULTS

- **Nominal concentrations:** 0, 100 (mg/L) and dispersant control.
- **Measured concentrations :** At start of the test (0 hr), <1.0, 80.6, <1.0(mg/L)
  At end of the test (72 hr), <1.0, 68.7, <1.0 (mg/L)
- **Unit :** mg/L
- **Results:** (calculated based on nominal concentrations)
  (1) **Growth inhibition (comparison of area under growth curve)**
  EC_{50} (0-72 h) > 100 mg/L
  NOEC (0-72 h)> 100 mg/L
  (2) **Growth inhibition (comparison of growth rates)**
  EC_{50} (24-48) > 100 mg/L
  EC_{50} (24-72) > 100 mg/L
  NOEC (24-72) > 100 mg/L
- **Was control response satisfactory:** Yes: Mean cell density increased to $270x10^6$ cells/mL (270-fold increase) after 72 hr for control. Mean cell density increased to $275x10^6$ cells/mL (275-fold increase) after 72 hr for Dispersant control.
- **Statistical results as appropriate:** Significant difference in the growth curve was not observed between values at 100 mg/L and in each control.

Remarks field for Results:

– Biological observations

Cell density at each flask at each measuring point:

Nominal Concentration (mg/L)	Cell Density ($x10^4$ cells/mL)			
	0 hr	24 hr	48 hr	72 hr
Control	1.0±0.00	6.5±0.50	50.5± 3.48	270.5±23.50
Dspersant Control	1.0±0.00	9.3±1.66	57.5± 9.39	275.2±17.22
1 00	1.0±0.00	16.1±7.82	65.1±12.82	283.3± 7.98

(Each value represents the mean of three sample counts.)

Growth curves: Logarithmic growth until end of the test (72 h).
Percent biomass/growth rate inhibition per concentration: Not described.
Observations: Test group(100mg/L) showed normal and similargrowth to that of control (283 fold increase after 72 hr).

CONCLUSIONS

(1)Growth inhibition(comparison of area under growth curve) EC_{50} (0-72 h) > 100 mg/L
NOEC (0-72 h) > 100 mg/L

(2)Growth inhibition(comparison of growth rates) EC_{50} (24-48) > 100 mg/L
EC_{50} (24-72) > 100 mg/L
NOEC (24-72) > 100 mg/L

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented. Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed:**
- **Order number forsorting:**
- **Remarks field for GeneralRemarks:**

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g., *DAPHNIA*) (1)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nuoplaz 6965

METHOD

- **Method:** ASTM and USEPA
- **Test type:** Flow-through condition
- **GLP:** Yes
- **Year:** 1984
- **Analytical procedures:** Yes. Measured by GLC, on 0,4,7,14,21day)
- **Species/Strain:** *Daphnia magna*
- **Test details:** Dynamic flow-through
- **Statistical methods:** ANOVA, 2WANOVA, arcsin transformation and Fisher's protected Least Significant Difference (LSD)

Remarks field for Test Conditions:

Test organisms: Source; in house culture
Age at study initiation: Juveniles within 24h old.
Control group: Yes (control and solvent control)

Test conditions: Dilution Solvent for Concentrated stock standards : Acetone (1.049mg/mL)
A proportional diluter system was used for the intermittent introduction of test material and dilution water into the test chambers.
Test temperature range: 18-22 °C (average temperature 20°C).
Well water was delivered to the chambers as a minimum rate of 2.0mL/min.
Exposure vessel type: 900mL test solution in a 1000 mL glass beaker; 4 beakers per treatment
Dilution water chemistry: Hardness and other characteristics are reported.
Dilution water pH in test: pH=8.3-8.4.
Lighting: 37-74 footcandles, 16h:8h light-darkness cycle
Feeding: Algae (Selenastrum capricornutum) three times a day
Supplemented with a trout chow suspension at least twice a week

Element (unit) basis: Mean cumulative numbers of juveniles produced per adult (reproduction)
Growth (length) of parental Daphnia
Long-term survival

Test design: Number of replicates=4; individuals per replicate=10;
Method of calculating mean measured concentrations:Geometric mean.

Exposure period: 21 d

Analytical monitoring: By GLC analysis. 33-101% of the nominal concentration atPreparation

RESULTS

- **Nominal concentrations:** 0, 0.0074, 0.012, 0.027, 0.048, 0.100 mg/L
- **Measured concentrations:**

Measured concentration of test chemical during 21-day exposure

Nominal concentration (mg/L)	Measured concentration (day, mg/L)					
	0	4	7	14	21	mean

Control	ND	ND	ND	ND	ND	ND
Solvent Cont.	ND	ND	ND	ND	ND	ND
0.0074	0.00328	0.00366	0.00558	0.00246	0.00482	0.0040
0.012	0.00748	0.00626	0.00843	0.00478	0.00747	0.0069
0.027	0.0172	0.0150	0.0204	0.0110	0.0157	0.0159
0.048	0.0305	0.0252	0.0371	0.0176	0.0348	0.029
0.100	0.0824	0.0766	0.0870	0.0630	0.1011	0.082

Cumulative Number of Dead Parental *Daphnia*.

Nominal conc.	Days									
(mg/L)	0	3	5	7	10	12	14	17	19	21
Control	0	0	0	0	0	0	0	1	1	2
Solvent Cont.	0	0	0	0	0	1	1	2	3	4
0.0074	0	0	0	0	0	1	1	1	1	1
0.012	0	0	0	0	0	0	0	0	0	0
0.027	0	0	0	0	0	0	0	0	0	0
0.048	0	0	0	0	1	1	1	1	1	1
0.100	0	0	0	0	0	0	0	0	0	0

Mean Growth data of Parental *Daphnia* (21-d)

Nominal conc. (mg/L)	Replicate A	Replicate B	Replicate C	Replicate D
Control	58.6 (n=9)	58.4 (n=9)	58.8 (n=10)	58.5 (n=10)
Solvent Cont.	59.1 (n=7)	59.0 (n=10)	59.0 (n=9)	59.3 (n=10)
0.0074	59.5 (n=10)	58.5 (n=10)	60.1 (n=9)	59.5 (n=10)
0.012	59.1 (n=10)	59.4(n=10)	59.5 (n=10)	59.8 (n=10)
0.027	59.8 (n=10)	58.4 (n=10)	59.9 (n=10)	60.3 (n=10)
0.048	59.6 (n=10)	59.6 (n-10)	59.7 (n=9)	58.6 (n=10)
0.100	58.7 (n=10)	60.0 (n=10)	58.8 (n=10)	59.0 (n=10)

Mean numbers of instar produced during 21-d.

Nominal conc.	Days									
(mg/L)	0	3	5	7	10	12	14	17	19	21
Control	-	-	-	-	109	196	317	86	179	170
Solvent Cont.	-	-	-	16	164	178		240	75	156
0.0074	-		-	3	141	202	302	261	75	274
0.012	-		-	3.5	122	206	373	221	96	265
0.027	-	-	-	8.3	150	189	317	218	138	313
0.048	-	-	-	-	113	203	242	120	233	214
0.100	-	-	-	5.3	135	186	223	180	93	269

Statistical results as appropriate:

Calculated LC_{50} Value for Parental *Daphnia:* LC_{50}(21day) >0.082(mg/L)

Calculated EC_{50} value for Inhibition of Reproduction: EC_{50}(21day) > 0.082(mg/L)

Remarks field for Results:

Biological observations

Cumulative numbers of dead parental *Daphnia*: Control: 2 (mortality: 5%).
Solv. Cont.: 4 (mortality: 10%)
0.0074 mg/L: 1 (mortality: 2.5%)
0.012 mg/L: 0 (mortality: 0%)
0.027 mg/L : 0 (mortality: 0%)
0.048 mg/L: 1 (mortality: 2.5%)

0.100 mg/ L : 0 (mortality: 0%)

Time of the first production of juveniles:Control : 7-10d
Solvent control: 5-7d
0.0074 mg/L : 5-7d
0.012 mg/L: 5-7d
0.027 mg/L : 5-7d
0.048 mg/L: 7-10d
0.100 mg/ L : 5-7d

Mean cumulative numbers of juveniles produced per adult alive for 21days:
Control : 112.7
Solvent control: 168.5
0.0074mg/L : 119.6
0.012 mg/L: 139.3
0.027 mg/L : 133.3
0.048 mg/L: 116.0
0.100 mg/L 112.9

Was control response satisfactory: Yes.

CONCLUSIONS

·NOEC (21-d, reproduction) : 0.082 mg/L,
·LOEC (21-d, reproduction) : >0.082 mg/L,
·EC_{50} (21-d, reproduction) : >0.082 mg/L;
·LC_{50} for parental *Daphnia* (21-d) : >0.082 mg/L

DATA QUALITY

- **Reliabilities:**
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Analytical Biochemistry Laboratories. Inc.,

REFERENCES

CMA Doc. I.D. 40-8565036 (1985).

OTHER

- **Last changed :**
- **Order number for sorting :**
- **Remarks field for GeneralRemarks :**

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g., *DAPHNIA*) (2)

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01 Purity: >95.0%

METHOD

• **Method:**	OECD TG 211 (revised edition of No.202).
• **Test type:**	Semi-static.
• **GLP:**	Yes
• **Year:**	1998
• **Analytical procedures:**	Yes. Measured by HPLC 2-3 times a week (before and after the replacement of the test water)
• **Species/Strain:**	*Daphnia magna*
• **Test details:**	Semi-static (water renewal: 3 times a week), open-system.
• **Statistical methods:**	Eco-Statics (Version 1.0 beta-edition R1.4)

Remarks field for Test Conditions:

Test organisms:	Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan). Age at study initiation: Juveniles within 24h old. Control group: Yes.
Test conditions	Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1.0wt.% (with solubilizer HCO-40 1.0wt.% controlled) with diluting water (Elendt M4) before use. Solubilizer concentration was controlled 100mg/L with working solution (HCO-40 1.0wt.%). Test temperature range: 19. 9-20.8 °C (average temperature 20°C). Exposure vessel type: 80mL test solution in a 100 mL glass beaker; 10 beakers per treatment Dilution water source: Elendt M4(OECD guideline No.211 Annex 2) Dilution water chemistry: Hardness: 251mg/L as $CaCO_3$ Lighting: <1 ,200 lx, 16h:8h light-darkness cycle Water chemistry in test: DO= 7. 0-9.2mg/L; pH=7.4-7.9. Feeding: *Chlorella regularis*, 0.1-0.2 mgC/day/individual
Element (unit) basis:	Mean cumulative numbers of juveniles produced per adult (reproduction)
Test design:	Number of replicates=10; individuals per replicate=10; Concentrations: 0, 55.6, and 100 mg/L, because 48h-EiC_{50} for parent Daphnia (Acute immobilization test) was>180mg/L. Dispersant control was also tested.
Method of calculating mean measured concentrations:	Geometric mean.
Exposure period:	21 d
Analytical monitoring:	By HPLC analysis. 99.7-101.3% of the nominal concentration at preparation; 94.7-99.3% just before the renewal of the test water (after 2 days exposure).

RESULTS

- **Nominal concentrations:** 0, 55.6, 100 mg/L
- **Measured concentrations:** Time-weighted measured concentrations of test chemical during a 21-day exposure were 54.8 and 98.7 mg/L.

Measured concentration of test chemical during 21-day exposure

Nominal concentration (mg/L)	Measured concentration (day, mg/L)					
	0(new)	2 (old)	7(new)	9(old)	16(new)	19(old)
Control	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0
Disp.Cont.	< 1.0	<1.0	< 1.0	< 1.0	< 1.0	< 1.0
55.6	56.3	54.4	55.4	53.9	56.3	52.6
100	100.4	99.3	100.0	98.5	99.8	95.2

new: freshly prepared test solutions.
old: test solution after 2 days exposure.

- **Unit :** mg/L
  - ·NOEC (21-d, reproduction) : 55.6 mg/L,
  - ·LOEC (21-d, reproduction) : >100 mg/L,
  - ·EC_{50} (21-d, reproduction) : 89.1 mg/L;
  - · LC_{50} for parental *Daphnia* (21-d) : >100 mg/L; calculated based on nominal concentrations.

Cumulative Number of Dead Parental *Daphnia*.

Nominal conc. (mg/L)	Days																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Disp.Cont.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
55.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	2	2

Mean cumulative numbers of juveniles produced per adult during 21-d.

Nominal conc. (mg/L)	Days																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.8	2.2	7.1	7.7	8.2	19.6	20.4	23.2	43.8	48.0	61.6	83.0	88.0	88.7
Disp.Cont.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.3	8.2	8.2	8.7	29.2	31.9	33.0	55.8	61.5	64.8	72.0	73.8	73.8
55.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.0	2.0	2.7	5.1	9.3	13.6	26.6	34.4	43.9	51.4	66.2	74.3	79.9
100	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	2.6	3.6	7.8	9.3	11.0	15.1	17.5	20.3	30.3	33.0	33.0

Cumulative Number of Juveniles produced per Adult Alive for 21-d.

Vessel No.	Cont.	Disp.Cont.	Nominal Concentration(mg/L) 55.6	100.0
1	74	74	68	37
2	57	71	70	25
3	126	92	65	-
4	127	78	96	-
5	90	73	89	36
6	84	70	116	29
7	71	76	78	35
8	94	84	93	28
9	78	75	87	34
10	86	45	37	40
Mean (S.D)	88.7(22.524)	73.8(12.072)	79.9(21.533)	33.0(5.127)
Inhibition rate(%)		0.832	0.901	0.372

Significant difference*1 **

-:were not calculated because the parental *Daphnia* was dead during a 21-days testing period.
1*:Indicates a significant difference by Dunnet multiple comparison procedure, Two-sides test.
**:Indicates a significant difference (alpha=0.01) from the control.

- **Statistical resultsas appropriate:**
  Calculated LC_{50} Value for Parental *Daphnia:* LC_{50}(21day) >100(mg/L)
  Calculated EC_{50} value for Inhibition of Reproduction: EC_{50}(21day) = 89.1(mg/L)
  (Statistical method: Logit)

Remarks field forResults :

Biological observations

Cumulative numbers of dead parental*Daphnia*: Control: 0 (mortality: 0%),
Disp.Cont.: 0(mortality: 0%)
55.6 mg/L: 0(mortality: 0%)
100 mg/L: 2 (mortality: 20%)

Time of the first production of juveniles: 8-13d for control
8-12d for dispersant control
8-13d for 55.6 mg/L
10-14d for 100 mg/L

Mean cumulative numbers of juveniles produced per adult alive for 21days:
Control: 88.7, Dispersant control: 73.8
55.6 mg/L: 79.9, 100 mg/L: 33.0

Was control response satisfactory: Yes. Mean cumulative numbers ofjuveniles produced per adult was 88.7 and 73.8 > 60.

CONCLUSIONS

- NOEC (21-d, reproduction) : 55.6 mg/L,
- LOEC (21-d, reproduction) : >100 mg/L,
- EC_{50} (21-d, reproduction) : 89.1 mg/L;
- LC_{50} for parental *Daphnia* (21-d) : >100 mg/L; calculated based on nominal concentrations.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed :**
- **Order number forsorting :**

- **Remarks field for GeneralRemarks:**

HEALTH ELEMENTS

ACUTE ORAL TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0%
  Kept at room temperature in a dark place until use. Stability of mixture of dose was confirmed for 7 days under 4C.

METHOD

- **Method:** OECD TG 401
- **Test type:** Single Dose Oral Toxicity Test
- **GLP:** Yes
- **Year:** 1996
- **Species:** Rat
- **Strain:** Crj: CD(SD)
- **Route of administration:** Oral (by single-dosegavage)
- **Doses/concentration levels:** 0(vehicle) and2,000 mg/kg
- **Sex:** Male & Female
- **Vehicle:** Corn oil
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
Age at study initiation: 6 weeks old for both sexes.
Weight at study initiation: 149-163 g for male.
126-140 g for female
No. of animals per sex per dose: 5 per sex per dose group

Study Design:
Vehicle: Corn oil. 40.0w/v% for 2000 mg/kg.
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
Each rat was weighed immediately prior to treatment,7 and 14 days after post-treatment observation period. The rats were observedeach hour to 6hr, after that, 2 times for one day during this time for signs of toxicity.

RESULTS

- **LD_{50}:** Male : > 2,000 mg/kg
  Female : > 2,000 mg/kg

REMARKS FIELD FOR RESULTS.

Body weight: The test substance did not cause any changes in body weight.
No detailed body weight data available.
Food/water consumption: No detailed data available.
Clinical signs : Loosening erring of the stool attributable to the treatment with corn oil was observed for 3 hours from the administration for both sexes in the groups given 0 and 2000 mg/kg. However, no deaths occurred of either male or female animals.
Haematology: Not done
Biochem: Not done.
Ophthalmologic findings: Not examined.
Mortality and time to death: No deaths were recorded in treated and control group.
Gross pathology incidence and severity: No macroscopic abnormalities that could be attributes to treatment with the test substance were seen on pathological examination.
Organ weight changes: Not done.
Histopathology (incidence and severity): Not done.

CONCLUSIONS

LD_{50} was established at > 2,000 mg/kg for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by the Biosafety Research Center, Food, Drugs and Pesticides (An-pyo Center), Japan

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.4(1996)

Ministry of Health & Welfare, Japan

GENERAL REMARKS

ACUTE INHALATION TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz 6959, Batch No. 39049
  Purity: 98.95%

METHOD

- **Method:** Not specified
- **GLP:** Yes
- **Year:** 1982
- **Species:** Rat
- **Strain:** Crj: CD(SD)
- **Doses/concentration levels:** 2,600 mg/m^3
- **Sex:** Male & Female
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:

Age at study initiation: Not stated.
Weight at study initiation: 210-275 g for both sexes.
No. of animals per sex per dose: 5 per sex per dose group

Study Design:

Inhalation Chamber: A 0.5m^3 stainless steel inhalation chamber was used. (Youg and Bertke, Cincinnati, Ohio)
The test compound atmosphere was generated directly into the chamber by means of Jet Nebulizer Mechanism. Chamberconcentrations were monitored by a filter paper/gravimetric techniqueapproximately every 30 min during the exposure period.
The HEPA filtered chamber air-flow was maintained between 10 to 20 air changes per hour during the exposure period with the chamber under slightly negative pressure.
The temperature in the chamber was maintained at 69-75 degree F with relative humidity of 30-50%
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
After the exposure, all animals were observed daily for 14 days for clinical signs of toxicity. Body weights were recorded prior to exposure and weekly thereafter. All animals were subjected to necropsy at termination of the study.

RESULTS

- **LD_0:** Male : > 2,600 mg/m^3

Female : > 2,600 mg/m³

REMARKS FIELD FOR RESULTS.

Body weight: The test substance did not cause any changes in body weight.

Mean body weight(g) of rats exposed to this chemical			
Males	Initial weight	265.1(8.48)	
	First week	297.8(14.02)	
	Second week	329.7(15.27)	
Females	Initial weight	213.9(2.66)	
	First week	223.2(3.96)	
	Second week	238.1(4.82)	Mean(S.D.)

Food/water consumption: No detailed data available.
Clinical signs : All animals (male and female) had matted, drenched coats for the first 2 days, otherwise no visible signs.
Haematology: Not done
Biochem: Not done.
Ophthalmologic findings: Not examined.
Mortality and time to death: No deaths were recorded.
Organ weight changes: Not done.
General necropsy observations: All males and 3/5 females exhibited reddening patches on lungs.

CONCLUSIONS

LD_0 was 2,600 mg/m³ for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by Midwest Research Institute.

REFERENCES

Nuodex Inc. Acute inhalation toxicity test in SpragueDawley rats using compoundNouplaz 6959

Environmental Protection Agency (1983)

GENERAL REMARKS

ACUTE DERMAL TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz 6959, Batch No. 39049
  Purity: 98.95%

METHOD

- **Method:** Procedure set forth in the Federal Insecticide, Fungicide, andRodenticide Act (FIFRA)
- **GLP:** Yes
- **Year:** 1981
- **Species:** Rabbits
- **Strain:** New Zealand albino white rabbits
- **Doses/concentration levels:** 2.0 mL/kg
- **Sex:** Male & Female
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:

Age at study initiation: Not stated.
Weight at study initiation: 2.3-3.2 kg for both sexes.
No. of animals per sex per dose: 3 per sex per dose group and 2 per sex for control.

Study Design:

Procedure: 24 hours prior to treatment the hair on the back of each rabbit was clipped so as to expose approximately 10% of the body surface area. Before dosing, epidermal abrasions were made longitudinally over the exposure area. The abrasions were sufficiently deep to penetrate the stratum corneum but not so deep as to cause bleeding.
A dosage was applied to the exposure area. A 2 x 2-inch gauze pad was placed on the exposure area to prevent seepage of the compound from the area. Each animal was then wrapped with a rubber dam. After 24 hour of exposure, the rubber dam and gauze pad were removed, and the exposure area was wiped to remove any remaining test material.
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
After the exposure, all animals were observed daily for 14 days for clinical signs of toxicity. A gross necropsy was performed on all animals at the end of the 14 day observation period.

RESULTS

- **LD_{50}:** Male : > 2.0 mL/kg
  Female : > 2.0 mL/kg

REMARKS FIELD FOR RESULTS.

Body weight: The test substance did not cause any changes in body weight.

Individual Animal Boy Weights

	Sex	Body weight (kg)		
Control		day 1	day 7	day 14
	male	3.2	3.4	3.6
		3.2	3.4	3.6
	female	2.7	3.0	3.1
		2.9	3.1	3.3
2.0 mL/kg	male	2.3	2.3	2.5
		2.4	2.4	2.5
		2.3	2.2	2.4
	female	2.3	2.5	2.7
		2.4	2.6	2.7
		2.4	2.5	2.6

Food/water consumption: No detailed data available.
Clinical signs : No toxic sign.
Haematology: Not done.
Biochem: Not done.
Ophthalmologic findings: Not examined.
Mortality and time to death: No deaths were recorded.
Organ weight changes: Not done.
Gross Pathology: Nothing noted.

CONCLUSIONS

LD_{50} was 2.0 mL/kg for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by Midwest Research Institute.

REFERENCES

Nuodex Inc. Acute dermal toxicity test of Tenneco Chemicals Inc. compound Nouplaz 6959 in rabbit.

Environmental Protection Agency (1981)

GENERAL REMARKS

SKIN IRRITATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz TOTM(Tenneco Chemicals, Inc.)
  Purity: 98.95%

METHOD

- **Method:** The test method was similar to Section 1500.41.Federal Hazardous Substances Act Regulations - 16 CFR
- **GLP:** Yes
- **Year:** 1981
- **Species:** Rabbits
- **Strain:** New Zealand albino white rabbits
- **Doses/concentration levels:** 0.5 mL
- **Sex:**
- **Post exposure observation period:** 24, 72 hours
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Husbandry Conditions Temperature - 70 ± 2 degree F
Relative Humidity - 45% ± 5%
Light - 12 hour light/dark cycle
Diet - Wayne 15% Rabbit Ration and tap water are provided ad libitum. Based on our current knowledge no contaminants are known to be in this diet or water that might be expected to interfere with the objectives of the study.
Caging - Stainless steel with elevated wire mesh flooring 1 rabbit/cage
Bedding - Techbord
Shepherd Products Company
Kalamazoo, Michigan 49005

Test method: A 0.5 mL portion of material was applied to an abraded and an intact akin site on the same rabbit. Gauze patches were then placed over the treated areas and an impervious material was wrapped snugly around the trunks of the animals to hold the patches in place.
The wrapping was removed at the end of the twenty-four (seventy two) hour period and the treated area were examined. TheDraize method of scoring was employed.

Evaluation: Draize Scale For Scoring Reactions

Erythema and Eschar Formation:	Value
No erythema	0
Very slight erythema(barely perceptible)	1
Well defined erythem	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slighteschar formation (injuries in depth)	4

Edema Formation	Value
No edema	0
Very slight edema(barely perceptible)	1
Slight edema(edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1millimeter)	3
Severe edema (raised more than 1 millimater and extending beyond the area of exposure)	4

RESULTS

- **Primary Irritation Score : 4.16/4 =1.04**

REMARKS FIELD FOR RESULTS.

	Reading	Rabbit Number						
Erythema and Eschar Formation	(Hours)	1	2	3	4	5	6	Average
Intact skin	24	2	1	2	1	2	1	1.50
Intact skin	72	0	0	1	0	0	0	0.17
Abraded skin	24	2	1	2	1	2	1	1.50
Abraded skin	72	0	0	1	1	0	0	0.33
						Subtotal		3.50
Edema Formation								
Intact skin	24	1	0	0	0	1	0	0.33
Intact skin	72	0	0	0	0	0	0	0.00
Abraded skin	24	1	0	0	0	1	0	0.33
Abraded skin	72	0	0	0	0	0	0	0.00
						Subtotal		0.66
						Total		4.16

CONCLUSIONS

Slightly irritating
This report concluded that TOTM was not a primary skin irritant in rabbit.
It is not possible to assign a classification.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1= reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by Biosearch Inc.

REFERENCES

Nuodex Inc. Primary Skin Irritation - Rabbits. OTS 2065758. Doc ID 878214470,1981

GENERAL REMARKS

EYE IRRITATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz TOTM(Tenneco Chemicals, Inc.)
  Purity: 98.95%

METHOD

- **Method:** The test method was similar to Section 1500.42.Federal Hazardous Substances Act Regulations - 16 CFR.
- **GLP:** Yes
- **Year:** 1981
- **Species:** Rabbits
- **Strain:** New Zealand albino white rabbits
- **Numbers of animals** 6
- **Doses/concentration levels:** 0.1 mL
- **Sex:**
- **Post exposure observation period:** 1,2,3,4,7 days
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Husbandry Conditions Temperature - 70 ± 2 degree F
Relative Humidity - 45%± 5%
Light - 12 hour light/dark cycle
Diet - Wayne 15% Rabbit Ration and tap water are provided ad libitum. Based on our current knowledge no contaminants are known to be in this diet or water that might be expected to interfere with the objectives of the study.
Caging - Stainless steel with elevated wire mesh flooring 1 rabbit/cage
Bedding - Techbord
Shepherd Products Company
Kalamazoo, Michigan 49005

Test method: 0.1 mL of the experimental material was instilled into the right eyes of the test animals while the other eyes remained untreated to severe as controls. The treated eyes were examined at one, two, three, four and seven days Following instillation of the test materials into the eyes.

Evaluation: Interpretation of the results was made in accordance with theDraize Scale of Scoring Ocular Lesions.

Scale of Scoring Ocular Lesions

	Value range
(1) CORNEA	
A. Opacity - Degree of Density(area most dense taken for reading)	0 - 4
B. Area of Cornea Involved	1 - 4
Score equals A x B x 5 (Total Maximum = 80)	
(2) IRIS	

A. Values 0 - 2

Score equals A x 5 (Total Maximum = 10)

(3) CONJUNCTIVAE

A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris) 0 - 3

B. Chemosis 0 - 4

C. Discharge 0 - 3

Score equals (A+B+C) x 2 (Total Maximum =20)

RESULTS

- **Average Ocular Irritation Score : 2.3(1 day), 1.7(2day), 0(3,4,7day)**

REMARKS FIELD FOR RESULTS.

Rabbit number	Tissue	Reading 1 day	2 day	3 day	4 day	7day
1	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
2	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	4	2	0	0	0
	Total Ocular Irritation Score	4	2	0	0	0
3	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
4	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
5	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
6	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	0	0	0	0
	Total Ocular Irritation Score	2	0	0	0	0
	Average Ocular Irritation Score	2.3	1.7	0.0	0.0	0.0

CONCLUSIONS

Slightly irritating

This report concluded that TOTM was not a primary skin irritant in rabbit.

It is not possible to assign a classification.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

Well conducted study, carried out by Biosearch Inc

REFERENCES

Nuodex Inc. Primary Eye Irritation - Rabbits. OTS 2065758. Doc ID 878214471,1983

GENERAL REMARKS

SENSITIZATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz TOTM(Tenneco Chemicals, Inc.)
  Purity: 98.95%

METHOD

- **Method:** Buehler teat
- **GLP:** Yes
- **Year:** 1981
- **Species:** Guinea pig
- **Strain:** Albino guinea pig
- **Numbers of animals** 10
- **Doses/concentration levels:** 0.5 mL
- **Sex:** male
- **Post exposure observation period:**10 application
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Husbandry Conditions Temperature – 70 ± 2 degree F
Relative Humidity– 45% ± 5%
Light – 12 hour light/dark cycle
Diet – Charless River Guinea Pig Furmula and tap water are provided ad Libitum. Based on our current knowledge no contaminants were Known to be in this diet or water that might be expected to Interfere with the objectives of the study.
Caging – Stainless steel with elevated wire mesh flooring 5 guinea pigs/cage
Bedding – Deotized Animal CageBoard(DACB)
Shepherd Products Company
Kalamazoo, Michigan 49005

Test method: A 0.5 mL portion of material was applied to the intact akin test site on the guinea pigs. A gauze patch was placed over the treated area and an impervious material was wrapped snugly around the trunks of the animals to hold the patches in place. After a 24 hour contact period the patch was removed and the animals were allowed to rest for one day. Following this rest period another application was applied to the same skin site using a fresh sample. After the tenth application the animals were rested for a two week period. At the termination of the rest period a challenge application was put on skin sites differing from the original test sites. The challenge application remained on for 24 hours.
The sites were examined for reaction using the Draize method of scoring to grade reactions.

Evaluation: Draize Scale For Scoring Reactions

Erythema and Eschar Formation:	Value
No erythema	0

Very slight erythema(barely perceptible)	1
Well defined erythem	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slighteschar formation(injuries in depth)	4

Edema Formation:	Value
No edema	0
Very slight edema(barely perceptible)	1
Slight edema(edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1millimeter)	3
Severe edema (raised more than 1millimater and extending beyond the area of exposure)	4

RESULTS

- **No sensitization**

REMARKS FIELD FOR RESULTS.

		Reading After Application number										Challenge	
Guinea pig No.		1	2	3	4	5	6	7	8	9	10	24hours	48hours
1	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
2	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
3	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
4	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
5	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
6	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
7	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
8	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
9	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
10	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0

CONCLUSIONS

No senstization

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

Well conducted study, carried out byBiosearch Inc.

REFERENCES

Nuodex Inc. Guinea Pig Contact Dermal Irritatiom/Sensitization-Modified Buehler Method *OTS 206574. Doc ID 878214475,1981*

GENERAL REMARKS

REPEATED DOSE TOXICITY (a)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nuoplaz 6959
  Purity: 98.2% (GC/FID) 97.9% (HPLC)
  Impurities were detected at level than 0.1-0.5%, one being di(2-ethylhexyl) phthalate (DEHP).

METHOD

- **Method:** BIBRA Standard Operating Procedures
- **Test type:** Repeat Dose Toxicity
- **GLP:** Yes
- **Year:** 1984
- **Species:** Rat
- **Strain:** Fischer 344
- **Route of administration** Oral
- **Doses/concentration levels:** 0(0), 0.2(184), 0.67(650) and 2(1826) % (mg/kg bw/day)
- **Vehicle:** Rodent diet
- **Sex:** Male & Female
- **Exposure period:** 28 days
- **Frequency of treatment:** Once daily
- **Control group and treatment:** Dietary level 0% and reference compound DEHP 0.67%.
- **Post exposure observation period:** None
- **Duration of test:** Males and females; for 28 days
- **Statistical methods:** The control and TOTM treated groups were subject to analysis of variance, and if this was significant the treated groups were compared with the controls using the Least Significant Difference test.
  The controls and DEHP groups were compared using a two-tailed pooled student t test with Welch's correction. In all cased a probability level of $P<0.05$ was taken to indicate statistical significance.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
Age at study initiation: 48-51 days old for males and females
Weight at study initiation: 137-154g for male.
111-132g for female.
No. of animals per sex per dose: 5 Rats per sex per dose group

Study Design:
Vehicle: Diet
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
Body wt. was recorded immediately prior to the first exposure and again for each animal 1, 3, 7, 10, 14, 17, 21, 24, 27 th days.
Twice each day the animals were observed in their cages forvariations in behaviour or condition, and once weekly a more detailed examination was made at the time of a weighing.

Food intakes were measured over the period day–3 to 0 and continuos intakes were measured at twice-weekly intervals until the day preceding autopsy. The intakes of test article or reference compound for each animal were calculated twice weekly using the analysed dietary concentrations of TOTM or DEHP, and the individual valued for bodyweight and food intake.

Hematologic parameters were evaluated for each animal. On the day preceding the start of the autopsies a sample of blood was collected from a caudal vein of each animal.

Autopsy: At the end of the 28th day treatment period the rats were deprived of food overnight, with water available. On the day of autopsy each animal was weighted and then killed. The blood was used to provide serum for clinical chemistry. During the autopsy any abnormalities of the external condition and of the thoracic or abdominal viscera were noted.

Organs: The weight of the following organs were recorded: adrenal glands, lungs, brain, ovaries, heart, spleen, kidneys, testes, liver, thyroid.

Electron microscopy: Two thin slices of liver, one from the left lobe, the other from the median lobe, were fixed for analysis. (The remainder of the liver was used for biochemical analysis.)

Biochemical analysis of the liver: Whole homogenates were prepared and assayed for protein and cyanide-insensitive palmitoyl-CoA.

RESULTS

- **NOAEL** 184 mg/kg bw
- **LOAEL** 650 mg/kg bw

REMARKS FIELD FOR RESULTS.

Body weight: No statistically significant differences of bodyweight between the control and TOTM or DEHP treated groups of either sex. There was a trend for the male rats from all the TOTM treated groups to be lighter than the controls. In the females, this trend was only evident in the 2.0% TOTM group.

Food/water consumption: Female rats fed 2.0% TOTM consumed significantly less diet than the controls during first seven days of treatment after which their intakes increased but remained lower than those of the controls. In the males there were no statistically significant differences between the control and TOTM fed groups during the treatment period.

Haematology : In both sexes haemoglobin concentration of the rats given diet containing 0.67 or 2.0% TOTM were statistically significantly lower than the control. In the males there was a small lowering of erythrocyte count in all groups given TOTM but this was not reproduced in the females.

Both sexes given the two higher dietary concentrations of TOTM had higher leucocyte counts than the control, but the differences were statistically significant only in the males. These male groups also had lower proportions of the leucocytes as eosinophils and monocytes.

Significantly lower values for haemotocrit and mean cell volume were limited to females given the two lower dose levels of TOTM.

Organ weights : In both sexes the liver weights, and liver weights relative to bodyweight, were

increased in the TOTM and DEHP treated animals compared to the controls. These differences were small and not statistically significant in the 0.2% TOTM group. The increase seen in the rats given2.0% TOTM was less than that in those given DEHP. In the males fed TOTM the higher values for brain weights relative to body weight, in the absence of any significant differences in the recorded weight probably reflect the lower bodyweights in the groups concerned. In the females there were statistically significant higher lung weights in the rats fed 0.2 or 0.67% TOTM when compered to the controls. In the case of the TOTM treatedanimals this difference was not dose related and not statistically significant when expressed relative to bodyweight.

Serum analyses : Analysis of serum from the males and females showed statistically significantly increased levels of albumin in the groups given 0.67 or 2.0% TOTM. In the males there were statistically significantly higher cholesterol levels in the 0.67 and 2.0% TOTM groups.

Concentrations of serum urea were statistically significantly increased in the male 2.0% TOTM group to the control values. In the females there was also an isolated statistically significantly lower value for lipid concentration in the 0.2% TOTM group.

Liver Biochemistry: Neither TOTM or DEHP treatment influenced to a statistically significant degree the concentration of hepatic protein. After TOTM treatmentPCoA activity was statistically significantly higher than controls in both sexes at the highest dose and in the males at the lower two doses. In the groups given TOTM only the highest dose level males had statistically significant increases of enzyme level. Both sexes given 0.67 or 2.0% TOTM had statistically significantly increased carnitine acetyltransferase activity with little difference between the two sexes.

Histology : No abnormalities were detected in themajority of the animals. The only lesions occurring with any frequency were focal interstitialpneumonitis and nephrocalcinosis in the females. The observations were not firmly dose related. Thepneumonitis was of limited extent, often only a single focus. Two female rats fed 2.0% TOTM showed reductions in sytoplasmic basophilia in liver although it was only marginal.

Electron Microscopy: In the hepatocytes from the control rats theperoxisomes varied in size from small to moderately large. They had uniformly electron dense contents and some possessed a lattice core. They were ubiquitously distributed throughout the cytoplasm. Feeding diet containing 2% TOTM produced a slight increase in the numbers of peroxisomes. which varied between cells. No difference was seen between the centrilobular and periportal areas.

CONCLUSIONS

The NOAEL for repeated dose toxicity is considered to be 184 mg/kg and the LOAEL is Considered 650 mg/kg for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

Well conducted study , carried out by the British Industrial Biological Research Associations

REFERENCES

Chemical Manufacturers Association, Project No. 3.0496. Report No. 0496/1/85

CMA Reference. TM-3.0-BT-BIB

GENERAL REMARKS

REPEATED DOSE TOXICITY (b)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use.

METHOD

- **Method:** Guidelines for 28-day Repeated Dose Toxicity Testing of Chemicals (Japan)
- **Test type:** Repeat Dose Toxicity
- **GLP:** Yes
- **Year:** 1996
- **Species:** Rat
- **Strain:** Crj:CD(SD)
- **Route of administration** Oral
- **Doses/concentration levels:** 0(vehicle) 100, 300 and 1,000 mg/kg/day
- **Vehicle:** Corn oil
- **Sex:** Male & Female
- **Exposure period:** 28 days
- **Frequency of treatment:** Once daily
- **Control group and treatment:** Vehicle (corn oil)
- **Post exposure observation period:** 2 weeks for 0 and 1,000 mg/kg/day dose.
- **Duration of test:** Males and females; for 28 days
- **Statistical methods:** Bartlett's test, Dunnett's test or Kruskal-Wallis test depending on whether or not the data were nonhomogeneous or homogeneous.
  Fisher 's test for the pathological result. Jonckheere's test for the correlation of dosage

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
Age at study initiation: 6 weeks old for males and females
Weight at study initiation: 130-151g for male.
110-121g for female.
No. of animals per sex per dose: 5 Rats per sex per dose group

Study Design:
Vehicle: Corn oil
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
Body wt. was recorded immediately prior to the first exposure and again for each animal every week
Hematologic parameters were evaluated for each animal. Bloodsamples for the hematologic determinations were taken fromabdominal artery in rats after 16 hr fast. Clinical chemistry analyses were performed on serum samples from each animal. Urinalyses were performed for each rat. Urine samples were collected from each rat on the day prior to scheduled termination.
Organs examined at necropsy:

Organ weight: brain, liver, kidney, spleen,adrenal, spemiary (male) and ovary (females) for each animal.
Microscopic: heart, liver, kidneys,spleen, adrenal and bone marrow from rats in the control and high-exposure groups and kidney from all dosage male.

RESULTS

- **NOAEL**

Male: >1,000 mg/kg/day
Female: >1,000 mg/kg/day

REMARKS FIELD FOR RESULTS.

Body weight: The mean body weight of treatment groups of rats for males and femalesnot Significantly different from controls at any time during the course of the study.
Food/water consumption: No significantly different from controls at any time during dosing and recoveringperiod for both sexes.
Clinical signs : No unusual clinical observations during the study.
Males: No dose-related change in general clinical signs.
Females: No dose-related change in general clinical signs.
Haematology :
at the end of dosing
Males and females: No dose-related significant changes inhematology.
In the blood clotting test, prothrombin times for males were slightly extended, but they were considered within the physiological change. For females, no significant changes in all test.
after recovering period
Males: In hematology, hemoglobin amounts for males at 1000mg/kg dosing were slightly increased, but they were considered within the physiological change. In the blood clotting test, no significant changes in all tests.
Females: No significant change in alltests.
Biochem :
at the end of dosing
Males: No dose-related significant adverse treatment-related effect in clinical chemistry.
Females: At 300, and 1,000 mg/kg dosing, chlorine contents were low.
after recovering period
Males: At 1,000 mg/kg dosing, potassium contents were slightly high.
Females: At 1,000 mg/kg dosing, GOT were slightly high.
But both changes were considered to be no meaning, because at the end of treatment these changes were not recognised
Urinalysis :
at the end of dosing
Males and Female: At 1,000 mg/kg dosing, some of rats (both sexes), amounts of urinary increased, but the mean urinary specificgravity values in the 1,000 mg/kg dosing group was not significant change from control group.
after recovering period:
Males and Females: No dose-related significant change in all tests.

Mortality and time to death: No deaths prior to scheduled termination.

Organ weight changes:

at the end of dosing

Male: No dose-related change in all tested organs.

Female: Relative liver weight were slightly increased at 100 mg/kg dosing, but no dose-related change. Other organs, no significant change.

after recovering period:

Males: At 1,000 mg/kg dosing, relative kidneyweight were slightly low.

Female: At 1,000 mg/kg dosing, absolute and relative adrenal weight wereslightly high.

But both changes were consideredno related to dosing and recovering of this chemical.

Gross pathlogy and histopathlogy:

at the end of dosing:

Males: Coloured patch/zone of lungs were observed 1 of 100 mg/kg, 2 of 300 mg/kg and 3 animals of 1,000 mg/kg dosing group. Also hypertrophy of the kidney, hypertrophy of parathyroid, and etc. were observed.
Amounts of eosinophilic body in the kidney were slightly increased in dosing group. But all these changes were considered no related the dosing and recovering of thischemical, because the degree and rate of changes were same of all the group included control.

Females: Red patch/zone of thymus dilated lumen of the uterus and etc. were observed. But all these changes were considered no related the dosing and recovering of this chemical, because the degree and rate of changes were same of all the group included control.

after recovering period:

Males and Females: No dose-related significant change in all tests.

CONCLUSIONS

No test substance related changes were noted in terms of clinical signs, body weight, food consumption, andhematology, blood chemicalexamination, urinalysis, and pathological findings.
The NOEL for repeated dose toxicity is considered to be 1,000 mg/kg/day for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study , carried out by the Biosafety Research Center, Food, Drugs and Pesticides (An-pyo Center), Japan

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.4(1996)
Ministry of Health & Welfare, Japan

GENERAL REMARKS

TOXICITY TO REPRODUCTION

TEST SUBSTANCE

- Identity: Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- Remarks: Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-80301
  Purity: >99.0% Kept at room temperature in a dark place until use.

METHOD

- **Method:** OECD Preliminary reproductive toxicity screening test
- **Test type:** Preliminary reproduction toxicity screening test.
- **GLP:** Yes
- **Year:** 1998
- **Species:** Rat
- **Strain:** Crj;CD (SD)
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0(vehicle) 100, 300, 1,000 mg/kg/day
- **Vehicle:** Corn oil
- **Sex:** Male & Female
- **Administration period:** Male; for 46 days from 2 weeks prior to mating
  Female; from 2 weeks prior to mating to day 3of lactation
- **Frequency of treatment:** Once daily.
- **Control group and treatment:** Vehicle (corn oil)
- **Post exposure observation period:** None.
- **Terminal kill** Male: day 47
  Female: day 4 of lactation
- **Statistical methods:** Chi square test for 1 grade positive data and Fisher's test for another. Bartlett's test or Kruskal-Wallis' test for 2 or more grade positive data. And used Dunnett's test or Mann-Whitney's U-test for examination

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:

***Age at study initiation*:** 10 week old for both sexes.
***Weight at study initiation*:** 373-435 g for males, 217-257 g for females
***No. of animals per sex per dose*:** 12 per sex per dose group

Study Design:

The animals were sacrificed on the day 4 of lactation for females. Males and females with nomated were killed1 day after the mating period. Females with no delivery killed 26th day of gestation period.
***Vehicle*:** Corn oil
***Satellite groups and reasons they were added*:** None
Mating procedures: Male/female per cage; 1/1, length of cohabitation;with in the limit of 14 days until proof of pregnancy (formation sperm detection in vagina) was observed.
Clinical observations performed and frequency:
Parent: General appearance once a day

Foetus: General appearance once a day after birth

Organs examined at necropsy:

Parent: Males and females: Grosspathlogy of all organs were tested.

Males: Organ weight: Testis and epididymis of all animals.

Female: Organ weight: Ovary of all animals.

Count: Implantation sites and corpusluteum of ovary of all animals.

Microscopic: Males: Testis and epididymis. Count ofsertoli sells, spermatocytes, round spermatids and elongatespermatids in seminiferous tubules of 5animals of all dosing groups.(Stage I-VI, VII-VIII, IX-XI, XII-XIV of spermatozoon formative cycle.)

Females: Ovary

Pup : Gross pathlogy of all organs were tested. Dead pups and abnormal organs were tested histopathogy.

***Parameters assessed during study*:**

Body weight. Males: Prior to the first dosing and 2, 5, 7, 10, 14 day. After that once a week, the daysacrificed. Females: Prior to the first dosing and 2, 5, 7, 10, 14 day. During gestation period, 0, 1,3, 5, 7, 10, 17 and 20 day. During lactation period, 0, 1, and 4. During cohabitationperiod, the same day with male.Pups: Day 0 and 4

Food/water consumption.The same day when body wt. determinedexcept lactation period and the day sacrificed for males, also, 0 day of gestation and lactation for female.

No. of pairs with successful copulation, copulation index (No.of pairs with Successful copulation/No. of pairs mated) x 100, duration of mating, No. of pregnant females, fertility index = (No.of pregnant animals/No. of pairs with successful copulation) x 100, No. of corpora lutea, No. of implantation sites, implantation index (No.of implantation sites/No. of corpora lutea) x 100, No. of pups born, delivery index (No.of pups born/No. of implantation sates)x 100, No. of love pups born, live birth index (No.of love pups born/No. of pups born) x 100, sex ratio of pups, No. of dead pups born, gestation length, gestation index (No. of females with live pops delivered/ Noof pregnant females) x 100, nursing index (No.of females nursing live pups/No.of females with normal delivery) x 100, No. of live pups on day 4, viability indcx (No.of live pups on day 4/No. of live pups born) x 100,

RESULTS

Repeat dose toxicity: NOEL 100 mg/kg/day for males
1,000 mg/kg/day for female

Reproductive and developmental toxicity: NOEL100 mg/kg/day for males
1,000 mg/kg/day for female
1,000 mg/kg/day for offspring

REMARKS FIELD FOR RESULTS.

Mortality and day of death : None.
Body weight : No statistical significant difference from controls.
Food/water consumption: No statistical significant difference from controls.

Reproductive data : No statistical significant difference from controls.

Pups data : Body weight and weight gain of 300 mg/kg dosing group for both sexes were slightly low. But all pups of 100 and 1000 mg/kg dosing group were not statistical significant difference from controls.

At the other tests, no statistical significant difference from controls.

Grossly visible abnormalities, external, soft tissue and skeletal abnormalities :

For males:

Slightly decrease of spermatocytes and spermatids: 2 animals of 300 mg/kg dosing group.
11 of 1000 mg/kg dosing group.

Moderate decrease of spermatocytes and spermatids: 1 of 1000 mg/kg/dosing group.
At this animal, a few multinucleate giant cell were appeared and slightly vacuolization of sertoli sells were observed. Also, at the epididymis, moderate amount of cell debris moderate decrease of spermatids and slightly granuloma of spermatic were observed.
For the control group, atrophy of seminiferous tubule were observed 2 animals. At these animals, slightly amount of cell debris were observedone of these animals, slight decrease of spermatids was also observed.

Number of cells in seminiferous tubules:

Group 1(Stage I-VI) : Low value of spermatids at 300 mg/kg dosing group.
Low values of spermatocytes and spermatids at 1000 mg/kg dosing group.

Group 2(Stage VII-VIII):Low values of round spermatids and ratio of sertoli cells at 1000 mg/kg.

Group 3(stage IX-XI) :Low values of elongate spermatids and ratio of sertoli cells at 1000 mg/kg.

Group 4(stage XII-XIV) :Low values of spermatocytes, elongate spermatids, and ratio of sertoli cells at 1000 mg/kg dosing group.

For females:

Cyst of corpus luteum of ovary was observed 2 animals of 300 mg/kg dosing group.

No abnormal ovary observed at the female of 100 mg/kg dosing without successful copulation, females of control and 100 mg/kg dosing without pregnant.

Histopathological finding in rats

		dose (mg/kg)			
Items		**0**	**100**	**300**	**1,000**
No. of male animals examined		12	12	12	12
Organ: Findings					
	Grade				
Testis:					
Decrease, spermatocyte and spermatid	**Total**	0	0	2	12**
	+	0	0	2	11
	+ +	0	0	0	1
Multinuclear giant cell, seminiferous tubule	+	0	0	0	1
Vacuolozation, Sertoli cell	+	0	0	0	1
Atrophy, seminiferous tubule	+	2	0	0	0
Epididymis:					
Cell debris, lumen	**Total**	2	0	0	1
	+	2	0	0	0
	++	0	0	0	1
Decrease, sperm	**Total**	1	0	0	1
	+	1	0	0	0
	++	0	0	0	1
Granuloma, spermatic	+	0	0	0	1

No. of female animals examined		12	12	12	12
Ovary:					
Cyst, corpus luteum	<+>	0	0	2	0

Values are no, of animals with finding.
Grade: +=slight, ++=moderate change and <+>=detected
Significantly different from 0 mg/kg group: **:p ≦0.01.

Number of cells in seminiferous tubules of male rats.

Items	dose (mg/kg) 0	100	300	1,000
No. of animals examined	5	5	5	5
Group 1 (Stage I-VI)				
No. of Sertoli cells	20.12(3.18)	19.08(1.49)	18.52(1.45)	18.08(1.45)
Spermatogonia				
No.	16.80(5.65)	20.52(2.58)	18.48(3.17)	15.76(2.61)
ratio [a]	0.85(0.29)	1.08(0.19)	1.01(0.21)	0.87(0.11)
Spermatocytes				
No.	50.80(7.44)	51.80(4.84)	42.64(2.63)	40.84(5.63)*
ratio	2.53(0.13)	2.72(0.26)	2.37(0.24)	2.25(0.16)
Round spermatids				
No.	138.36(17.20)	128.00(8.89)	117.68(5.59)*	112.60(3.11)**
ratio	6.91(0.35)	6.75(0.84)	6.39(0.70)	6.26(0.48)
Elongate spermatids				
No.	130.00(21.71)	132.32(11.17)	103.28(12.34)*	95.36(8.44)**
ratio	6.53(1.15)	6.98(0.88)	5.62(0.90)	5.30(0.69)
Group 2 (Stage VII-VIII)				
No. of Sertoli cells	16.96(2.63)	17.04(2.17)	16.64(2.73)	16.52(2.23)
Spermatogonia				
No.	2.92(1.06)	2.40(0.93)	2.04(0.68)	2.60(1.10)
ratio	0.18(0.09)	0.14(0.05)	0.12(0.03)	0.16(0.06)
Spermatocytes				
No.	91.68(10.37)	94.68(6.55)	84.44(6.99)	82.32(6.70)
ratio	5.45 (0.56)	5.60(0.51)	5.16(0.79)	5.03(0.54)
Round spermatids				
No.	142.08(13.39)	131.64(13.72)	123.96(8.23)	118.76(8.28)*
ratio	8.45(0.62)	7.75(0.39)	7.66(1.66)	7.25(0.62)*
Elongate spermatids				
No.	129.24(17.37)	128.32(16.88)	114.72(9.80)	105.65(13.47)
ratio	7.78(1.54)	7.56(0.72)	7.09(1.62)	6.46(1.05)
Group 3 (Stage VII-VIII)				
No. of Sertoli cells	19.28(1.92)	20.52(1.55)	19.20(1.58)	19.32(2.18)
Spermatogonia				
No.	4.52(1.32)	4.20(1.50)	4.92(1.63)	3.32(1.02)
ratio	0.23(0.05)	0.21(0.08)	0.26(0.11)	0.18(0.05)
Spermatocytes				
No.	102.52(10.83)	99.08(8.42)	97.56(4.50)	89.04(9.00)
ratio	5.34(0.56))	4.85(0.50)	5.10(0.36)	4.62(0.32)
Elongate spermatids				
No.	145.24(11.01)	130.64(9.90))	131.68(19.71)	119.24(15.90*
ratio	7.56(0.61)	6.37(0.23)	6.88(1.04)	6.21(0.83)*

Group 4 (Stage VII-VIII)				
No. of Sertoli cells	19.16(2.81)	20.92(1.73)	18.64(1.72)	16.72(0.92)
Spermatogonia				
No.	4.04(0.89)	3.72(0.72)	3.64(0.48)	3.64(0.71)
ratio	0.21(0.05)	0.18(0.03)	0.20(0.02)	0.22(0.05)
Spermatocytes				
No.	109.80(13.15)	110.36(9.22)	99.44(4.54)	88.76(4.33)**
ratio	5.76 (0.29)	5.28(0.12)	5.36(0.34)	5.32(0.46)
Elongate spermatids				
No.	159.76(15.91)	150.28(18.99)	137.08(17.70)	105.16(18.34)**
ratio	8.39(0.63)	7.19(0.71)	7.35(0.62)	6.33(1.31)**

Values are expressed as Mean(S.D.)

Significantly different from 0 mg/kg group; * $p \leqq 0.05$, ** $p \leqq 0.01$

a): (No. of spermatogenic cells/no. of sertoli cells in a seminiferous tubule)

Influence on reproductive performances of rats

	dose (mg/kg)			
Items	**0**	**100**	**300**	**1,000**
No. of male animals examined	12	12	12	12
No. of pairs with successful copulation	12	12	12	12
Duration of mating (day, Mean, (SD))	2.1(1.2)	2.3(1.3)	2.7(1.2)	2.7(1.1)
Copulation index(%)*	100.0	91.7	100.0	100.0
No. of pregnant animals	11	10	12	12
Fertility index(%)**	91.7	90.9	100.0	100.0

*(No.of pairs with successful copulation/no.of pairs mated) x 100

**(No. of pregnant animals/no.of pairs with successful copulation) x 100

Influence on developmental performances of rats

	dose (mg/kg)			
Items	**0**	**100**	**300**	**1,000**
No. of male animals examined	12	12	12	12
No. of corpora lutea	16.8(1.5)	17.3(1.3)	17.0(2.3)	17.9(2.2)
No. of implantation sites	15.5(1.7)	16.6(1.3)	16.0(2.0)	16.3(2.3)
Implantation index(%) [a]	92.5(7.2)	96.2(6.6)	94.5(8.4)	91.3(8.8)
No. of pups born(%)	13.7(3.1)	15.0(1.7)	15.0(1.8)	15.1(2.7)
Delivery index(%) [b]	87.6(15.4)	90.3(6.8)	94.1(7.2)	92.2(9.6)
Live pups born				
No.	13.3(2.9)	14.7(2.0)	14.9(2.0)	15.0(2.7)
Live birth index(%) [c]	97.1(5.6)	97.8(3.6)	99.2(2.6)	99.4(2.1)
Sex ratio(M/F)	1.09(0.69)	1.05(0.50)	1.17(0.75)	0.76(0.44)
Dead pups born				
No.	0.5(0.9)	0.3(0.5)	0.1(0.3)	0.1(0.3)
Gestation length(day)	22.7(0.5)	22.7(0.5)	22.5(0.5)	11.6(0.5)
Gestation index(%) [d]	100.0	100.0	100.0	100.0
Nursing index(%) [e]	100.0	100.0	100.0	100.0
Live pups on day 4				
No.	13.2(2.8)	14.6(2.1)	14.4(2.9)	14.5(2.9)
Viability index(%) [f]	99.5(1.8)	99.3(2.3)	95.6(11.5)	96.7(6.7)
Body weight of pups(g)				
Male Day 0	7.32(0.77)	7.13(0.52)	6.69(0.55)	6.87(0.84)
Day 4	11.71(1.76)	11.09(0.93)	10.23(0.98)*	10.60(1.47)
Day 0-4, gain(g)	4.39(1.04)	3.96(0.53)	3.54(0.77)*	3.73(0.80)
Body weight gain(%) [g]	59.41(8.87)	55.54(6.16)	53.19(11.91)	54.39(9.50)

Female	Day 0	6.93(0.83)	6.63(0.64)	6.33(0.58)	6.58(0.62)
	Day 4	11.08(1.71)	10.28(1.01)	9.84(1.01)*	10.03(1.46)
	Day 0-4, gain(g)	4.16(1.00)	3.65(0.56)	3.14(0.79)*	3.46(0.96)
	Body weight gain(%)	59.63(10.42)	55.24(8.07)	49.95(13.09)	52.17(11.10)

Values are expressed as Mean (S.D.)
Significantly difference from 0 mg/kg group ; $p \leqq 0.05$
a): (No. of implantation sites/no. of corpora lutea) x 100
b): (No. of pups born/no. of implantation sites) x 100
c): (No. of live pups born/no. of pups born) x 100
d): (No. of females with live pups delivered/ no. of pregnant females) x 100
e): (No. of females nursing live pups/no. of females with normal delivery) x 100
f): (No. of live pups on day 4/ no. of live pups born) x 100
g): (Body weight gain/body weight on day 0) x 100

CONCLUSIONS

Repeat dose toxicity

Histopathological examination of the testes, demonstrated decrease ofspermatocytes and spermatids in males of the 300 and 1000 mg/kg group. No effects of this chemical on general appearance, body weight, food consumption, autopsy findings, weights of the reproductive organs of both sexes, or histopathlogical features of the ovary were detected.

The NOELs are considered to be 100 mg/kg/day for males, and 1,000 mg/kg/day for females.

Reproductive and developmental toxicity

Except for the effects in males observed onhistopathological examination, no influence of this chemical was detected regarding reproductive ability, organ weight onhistopathological feature of the ovary, delivery or maternal behaviour of dams. No effects of this chemical were detected onviability, general appearance, body weights or autopsy findings for offspring.

The NOELs are considered to be 100 mg/kg/day for males, 1,000 mg/kg/day for females, and 1,000 mg/kg/day for offspring.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study , carried out by the Safety Research Institute for Chemical Compounds Co., Ltd.(Japan)

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.6(1998)

Ministry of Health & Welfare, Japan

GENERAL REMARKS

GENETIC TOXICITY IN VITRO (BACTERIAL TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use.

METHOD

- **Method:** Guideline for ScreeningMutagenicity Testing of Chemicals(Japan) and OECD TG 471 and 472
- **Test type:** Reverse mutation assay
- **GLP:** Yes
- **Year:** 1996
- **Species/Strain:** *Salmonella typhimurium* TA100, TA1535, TA98, TA1537
  Escherichia coli WP2 *uvr*A
- **Positive controls:** -S9 mix, 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, WP2, TA98)
  Sodium azide (TA1535)
  9-Aminoacridine (TA 1537)
  +S9 mix, 20Aminoanthracene (five strains)
- **S9:** Rat liver, induced withphenobarbital and 5,6-benzoflavone
- **Statistical methods** No statistical analysis was done.

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

Concentration: -S9: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (five strains)
+S9: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (five strains)
Number of replicates: 2
Plates/test: 3
Procedure: Plate incorporation method
Solvent: Acetone
Positive controls:
-S9 mix, 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, WP2, TA98)
Sodium azide (TA1535)
9-Aminoacridine (TA 1537)
+S9 mix, 20Aminoanthracene (five strains)

RESULTS

- **Cytotoxic concentration:**

Toxicity was not observed up to 5,000 ug/plate in five strains with and without metabolic activation (S9 mix).

- **Genotoxic effects:**

	+	?	-
With metabolic activation:	[ ]	[ ]	[x]
Without metabolic activation:	[ ]	[ ]	[x]

REMARKS FIELD FOR RESULTS.

CONCLUSIONS

Bacterial gene mutation is negative with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** Valid without restriction.

Remarks field for Data Reliability

Well conducted study, carried out by Hatano Research Institute, Food and Drug Safety Center (Hadano, Japan).

REFERENCES

Toxicity Testing Reports of Environmental Chemicals, vol.4 (1996)

Ministry of Health & Welfare, Japan

GENERAL REMARKS

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use

METHOD

- **Method:** Guideline for Screening Toxicity Testing ofChemicals (Japan)
- **Test type:** Chromosomal aberration test
- **GLP:** Yes
- **Year:** 1996
- **Species/Strain:** CHL/IU cell
- **Metabolic activation:** with and without S9 from rat liver, induced withphenobarbital and 5,6-benzoflavone.
- **Statistical methods** Fisher's exact analysis

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

For continuous treatment, cells were treated for 24 or 48 hrs without S9.
For short-term treatment, cells were treated for 6 hrs with and without S9 and cultivated with fresh media for 18 hrs.

Concentration: -S9 (continuous treatment): 0, 1.3, 2.5, 5.0 mg/mL
-S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
+S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
Plates/test: 2
Solvent: Acetone
Positive controls: Mitomycin C for continuous treatment
Cyclophosphamide for short-term treatment

RESULTS

- **Cytotoxic concentration:**

Toxicity was not observed up to 5.0 mg/ml in continuous and short-term treatment with or without S9 mix.

- **Genotoxic effects:**

	Clastogenicity			polyploidy		
	+	?	-	+	?	-
With metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]
Without metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]

REMARKS FIELD FOR RESULTS.

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use

METHOD

- **Method:** Guideline for Screening Toxicity Testing ofChemicals (Japan)
- **Test type:** Chromosomal aberration test
- **GLP:** Yes
- **Year:** 1996
- **Species/Strain:** CHL/IU cell
- **Metabolic activation:** with and without S9 from rat liver, induced withphenobarbital and 5,6-benzoflavone.
- **Statistical methods** Fisher's exact analysis

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

For continuous treatment, cells were treated for 24 or 48 hrs without S9.
For short-term treatment, cells were treated for 6 hrs with and without S9 and cultivated with fresh media for 18 hrs.

Concentration: -S9 (continuous treatment): 0, 1.3, 2.5, 5.0 mg/mL
-S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
+S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
Plates/test: 2
Solvent: Acetone
Positive controls: Mitomycin C for continuous treatment
Cyclophosphamide for short-term treatment

RESULTS

- **Cytotoxic concentration:**

Toxicity was not observed up to 5.0 mg/ml in continuous and short-term treatment with or without S9 mix.

- **Genotoxic effects:**

	Clastogenicity			polyploidy		
	+	?	-	+	?	-
With metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]
Without metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]

REMARKS FIELD FOR RESULTS.

Appendix I
Parameters used in caluculation of distribution by Mackay level III fugacity model.

Physico-chemical Parameter for TOTM

molecular weight		546.79	Measured
melting point [°C]		-50	Measured
vapor pressure [Pa]		2.80E-04	Estimated
water solubility [g/m³]		0.13	Measured
log Kow		5.94	Measured
half life [h]	in air	12	Estimated
	in water	288	Estimated
	in soil	288	Estimated
	in sediment	864	Estimated

Temp. [°C] 25

Environmental Parameter

		Volume [m³]	depth [m]	area [m²]	organic carbon [—]	lipid content [—]	density [kg/m³]	residence time [h]
bulk air	air	1.0E+13					1.2	100
	particles	2.0E+03						
	total	1.0E+13	1000	1E+10				
bulk water	water	2.0E+10					1000	1000
	particles	1.0E+06			0.04		1500	
	Fish	2.0E+05				0.05	1000	
	Total	2.0E+10	10	2E+09				
bulk soil	Air	3.2E+08					1.2	
	Water	4.8E+08					1000	
	Solid	8.0E+08			0.04		2400	
	Total	1.6E+09	0.2	8E+09				
bulk sediment	Water	8.0E+07					1000	
	Solid	2.0E+07			0.06		2400	50000
	Total	1.0E+08	0.05	2E+09				

Intermadea Transport Parameter (m/h)

air side air-water MTC	5	soil air boundary layer MTC	5
water side air water MTC	0.05	sediment-water MTC	1E-04
rain rate	1E-04	sediment deposition	5E-07
aerosol deposition	6E-10	sediment resuspension	2E-07
soil air phase diffusion MTC	0.02	soil water runoff	5E-05
soil water phase diffusion MTC	1E-05	soil solid runoff	1E-08

Theoretical Distribution of TOTM

scenario 1

	emission rate [kg/h]	conc. [g/m^3]	amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
Air	1,000	1.3.E-07	1.3.E+04	19.6	7.5E+02	1.3.E+02
Water	0	1.6.E-05	3.10.E+03	4.7	7.6E+00	3.1.E+00
Soil	0	2.5.E-03	4.4.E+04	66.2	1.1E+02	
Sediment		1.3.E-02	6.3.E+03	9.5	5.1E+00	1.2.E-01
		total amount	6.7.E+04			

scenario 2

	Emission rate [kg/h]	conc. [g/m^3]	Amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
air	0	1.8.E-09	1.8.E+02	0.0	1.0.E+01	1.8.E+00
water	1000	9.7.E-04	1.9.E+05	32.7	4.7.E+02	1.9.E+02
soil	0	3.4.E-05	6.2.E+02	0.1	1.5.E+00	
sediment		7.9.E-01	3.9.E+05	67.2	3.2.E+02	7.9.E+00
		total amount	5.9.E+05			

scenario 3

	emission rate [kg/h]	conc. [g/m³]	Amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
air	0	7.0.E-13	7.0.E-02	0.0	4.1.E-03	7.0.E-04
water	0	5.2.E-08	1.0.E+01	0.0	2.5.E-02	1.0.E-02
soil	1000	2.3.E-02	4.2.E+05	100.0	1.0.E+03	
sediment		4.2.E-05	2.1.E+01	0.0	1.7.E-02	4.2.E-04
		total amount	4.2.E+05			

scenario 4

	emission rate [kg/h]	conc. [g/m³]	Amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
air	600	7.8.E-08	7.8.E+03	3.0	4.5.E+02	7.8.E+01
water	300	3.0.E-04	6.0.E+04	23.5	1.5.E+02	6.0.E+01
soil	100	3.8.E-03	6.8.E+04	26.6	1.6.E+02	
sediment		2.4.E+01	1.2.E+05	46.9	9.8.E+01	2.4.E+00
		total amount	2.6.E+05			

Summary of SIDS Information on Trimellitates
A. Physical/Chemical Properties of Trimellitates

(R) Carbon Chain Length	CAS Number	Chemical Name	MP* (°C)	BP** (°C)	VP (hPa@25°C)	PC (log Pow)	Water Solubility (mg/L @25°C)	Photodeg Half-life (days)	Hydrolysis Half-life (yrs)	Transport (%) c			
										Soil	Air	Water	Sediment
C8	3319-31-1	tris 2-ethylhexyl (TOTM)	-46 97 c	>300 541 c	<0.0001*** 5.25E-11 c	5.94 11.59 c	3.9E-04 4.51E-08 c	0.33 c	0.05 0.32 c	97.8	3.6E - 6	2.8E - 7	2.17
C8	27251-75-8	triisooctyl ester	<0 197 c	541 c	5.25E-11 c	11.59 c	4.51E-08 c	0.35 c	0.43 c	97.8	3.64E - 6	2.8E - 7	2.17
C9	53894-23-8	triisononyl ester	<0 224 c	>300 575 c	3.17E-12 c	13.06 c	1.32E-09 c	0.31 c	0.86 c	97.8	2.74E - 7	9.61E -9	2.17
C8,C10	67989-23-5	decyl, octyl ester	<0 234 c	585 c	1.37E-12 c	12.79 c	2.78E-09 c	0.32 c	0.98 c	97.8	1.02E - 7	1.79E - 8	2.17

c = calculated data using EPWIN; all other values are derived from measurements

* = All of these trimellitates are liquids at zero degrees C. Modeled data do not accurately reflect melting points for these substances

** = Measured boiling points were determined to be >300°C at 0.66 kPa

*** = vapor pressure of TOTM 13 Pa @ 200°C

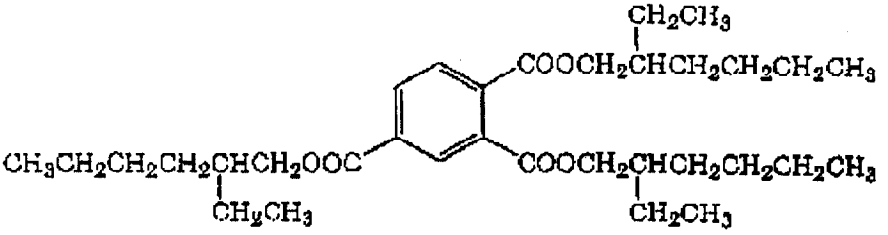
Summary of SIDS Information on Trimellitates
B. Toxicology Data on Trimellitates

(R) Carbon Chain Length	CAS Number	Chemical Name	Acute Oral LD50	Acute Dermal LD50	Acute Inhalation LC50	Repeated Dose Toxicity	GeneTox (Ames)	GeneTox (Chrom. Abs.)	Toxicity to Reproduction	Developmental Toxicity / Teratogenicity	Acute Fish (A) mg/L	Daphnia (B) mg/L	Algal (C) mg/L	Biodegradation %
C8	3319-31-1	tris 2-ethylhexyl (TOTM)	> 3.2 g/kg (rat, mouse)	>20 ml/kg (guinea pig) >2.0 ml/kg (rabbit)	<2.64 mg/L (rat, nominal)	NOAEL (rat, dietary) 654 mg/kg/day	Negative	Negative (CHL/IU cells)	NOAEL (rat, oral) 1000 mg/kg/day	NOAEL (rat, oral) 1000 mg/kg/day (3)	>100	>180	>100	68-71 (1) 4.2 (2)
C8	27251-75-8	Triisooctyl ester												
C9	53894-23-8	Triisononyl ester	> 10 g/kg (rat)											
C8, C10	67989-23-5	decyl, octyl ester												

Footnotes: A) Japanese Medaka (*Oryzias latipes*), 96 hr LC50 & NOEC
B) *Daphnia magna*, 48-hr EC50
C) *Selenastrum capricornutum*, 72-hr EC50 & NOEC

(1) Inherent biodegradation by Shake Flask Method
(2) Ready biodegradation by MITI method (OECD 301C)
(3) OECD Preliminary reproduction toxicity screening test; indirect measure of develomental effects

SIDS INITIAL ASSESSMENT PROFILE

CAS NO.	3319-31-1
CHEMICAL NAME	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
Structural formula	

RECOMMENDATION

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human health

Acute toxicity of TOTM is low; LD_{50} >2,000 mg/kg in rats. In the irritation-test for animals, this substance is slightly irritating to the skin and the eyes. Sensitization test on guinea pig showed"no sensitization". Oral study in rats conducted for 28 days at doses of0(0), 0.2(184), 0.67(650), 2.0(1826) % (mg/kg bw/day) of TOTM. There were no statistically significant differences in body weights between control andTOTM treated groups. There was a significant difference between control and treated groups in thefollowing: hemoglobin concentration (lower in both sexes, 0.67 or 2.0% TOTM), leucocyte counts (higher in males at 0.67 or 2.0%), absolute and relative liver weights (higher in both sexes at all levels except 0 or 0.2%),serum albumin (higher in both sexes at 0.67 or 2.0%), serum cholesterol levels (higher in males at 0.67 or 2.0%), serum urea (higher in males at 2.0%), serum lipids (decreased in females at0.2%). Liver biochemistry revealed statistically significant differences between treated and control groupsas indicated by palmitoyl CoA oxidation (increased in both sexes at 2.0% and males at all dose levels), and catalase activity (increased in males at 2.0%).

Preliminary reproductive toxicity screening test reveals moderate decrease ofspermatocytes and spermatids in males at 100mg/kg/day. From these two test results, he NOAELs for repeated oral toxicity were considered to be100 mg/kg/day for male rats. The NOAELs for reproductive/ developmental toxicity were considered to be1,000 mg/kg/day for female rats and for offspring.

TOTM was evaluated its genotoxicity by many assay systems. It was neithermutagenic in bacteria nor clastogenic in mammalian cells*in vitro*. All other *in vitro* and *in vivo* assays gave negative results. It is concluded that TOTM is not genotoxic *in vitro* and *in vivo*. The reported results of carcinogenecity was invalid.

Absorption and metabolism were studied for ^{14}C labeled TOTM and about 75% of the dose was excreted unchanged in the feces, 16% in the urine as metabolites and 1.9% was expired as $^{14}CO_2$.

Environment

The Mackay level III fugacity Model was employed to estimate the environmental distribution of TOTM in air, water, soil and sediment. If released to air, TOTM will exist solely in the particulate phase in the ambient atmosphere. If released to soil, TOTM is not expected to have mobility. If released into water, TOTM is expected to adsorb to suspended solids and sediment in water.

TOTM has to be considered as weakly toxic against aquatic organisms. The substance is not readily biodegradable. Measured BCF of this chemical is reported as less than 1 to 2.7 in carp for 6 weeks, which suggest that bioconcentration in aquatic organisms is much lower than the value estimated from logPow(=5.94). The toxicity data to aquatic plants (algae; *Selenastrum capricornutum*) was >100 mg/L for EC_{50} (72hr) and NOEC (72hr). The acute toxicity data in fish (medaka; *Oryzias latipes*) were >100 mg/L (96h, LC_{50} and NOEC) and >75 mg/L (14d, LC_{50} and NOEC). In *Daphnia magna*, acute toxicity was >180mg/L (48hr: EC_{50}) and chronic toxicity was 55.6mg/L (21d, reproduction NOEC). All these data were obtained in supersaturated solution with the aid ofsolubilizer (HCO-40). The test solution was considered to be homogeneous substantially. Another chronic toxicity data in*Daphnia magna* (NOEC >0.082mg/L) was reported. Though this value is lower than the saturation point, the observed concentration data was less reliable. Assessment factor of 100was chosen to determinethe lowest PNEC. Thus, calculated PNEC (=0.00082 mg/L) of TOTM is closely to the value of one hundredths (assessment factor) of saturation point. From these toxicity data, it is difficult to decide the exact PNEC, but we are sure of the practical safety of TOTM against aquatic organisms.

Exposure

TOTM is manufactured as the plasticizer of PVC applications.
The production volume of TOTM in Japan is approximately 20,000 tonnes/year and also, there are 5 manufacturers in Japan. Estimated global production is 40,000-100,000 tonnes/year. This substance is produced in closed system and mainly used asplasticizer for PVC electrical cable and wire. And so, this substance has been already blended to the compound asplasticizer, so it is not expected that downstream users or consumers of electric wire industry may expose to this substance.

Occupational exposure may occur through dermal contact and inhalation of mist. The process is constructed by closed system and workers wear protective gloves and goggles during the operation, so significant exposure is not expected.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation

FULL SIDS SUMMARY

CAS NO: 3319-31-1		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		OECD TG 102	< - 50 °C (223 K)
2.2	Boiling Point		Other (unknown)	283 °C (at 4 hPa)
2.3	Density		Other (unknown)	0.987-0.990 g/cm^3 at 20 °C
2.4	Vapour Pressure		OECD TG 104	< 2.8 x 10^{-4} Pa at 100 °C
2.5	Partition Coefficient (Log P_{ow})		OECD TG 107	5.94 at 25 °C
2.6A.	Water Solubility		OECD TG 105	0.13 mg/L at 25 °C
B.	pH			None
	pKa			None
2.12	Oxidation: Reduction Potential			None
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation			None
3.1.2	Stability in Water		OECD TG 111	Stable at pH 4 at 50°C $T_{1/2}$=17.5 days at pH 7 at 25°C $T_{1/2}$=11.9 days at pH 9 at 25°C
3.2	Monitoring Data			None
3.3	Transport and Distribution		Calculated (Level III Fugacity Model)	(Release 100% to air) Air Water Soil Sediment 19.6% 4.7% 66.2% 9.5% (Release 100% to water) Air Water Soil Sediment 0.0% 32.7% 0.1% 67.2% (Release 100% to soil) Air Water Soil Sediment 0.0% 0.0% 100% 0.0%
			(local exposure)	PEC_{local} = None
3.5	Biodegradation		OECD TG 302C	4.2 % after 28 days
3.7	Bioaccumulation		OECD TG 305C	BCF=1-2.7(Conc. 0.2 mg/L)
ECOTOXICOLOGY				
4.1 A	Acute Toxicity to Fish	*Oryzias Latipes*	OECD TG 203	LC_{50} (96 hr) > 100 mg/L
4.1 B	Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 204	LC_{50} (14 day) > 75 mg/L NOEC(14 day) > 75 mg/L LOEC(14 day) > 75 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50} (24 hr) > 180 mg/L EC_{50} (48 hr) > 180 mg/L NOEC > 180 mg/L LOEC > 180 mg/L
4.3	Toxicity to Aquatic Plants e.g. *Algae*	*Selenastrum Capricornutum* ATCC22662	OECD TG 201	EC_{50} (72 hr) > 100mg/L NOEC(72 hr) > 100mg/L
4.5.1	Chronic Toxicity to Fish			None

4.5.2	Chronic Toxicity to Aquatc Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 211	NOEC(21d,reproduction)= 55.6 mg LOEC(21d,reproduction)>100mg/L EC_{50}(21d, reproduction) >89.1mg/L LC_{50} for parental *Daphnia*(21d)>100 mg/L NOEC=0.0082 (21d, reproduction, parent *Daphnia* mortality)
4.6.1	Toxicity to Soil Dwelling Organisms			None
4.6.2	Toxicity to Terrestrial Plants			None
4.6.3	Toxicity to Other Non- Mammalian Terrestrial Species (Including Birds)			None
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	OECD TG 401	LD_{50} > 2,000 mg/kg (for both sexes)
5.1.2	Acute Inhalation Toxicity	Rat	Other	2,600 mg/m^3 (4hr)
5.1.3	Acute Dermal Toxicity	Rabbit	Other	LD_0 > 2.0 mL/kg
5.2.1	Skin Irritation	Rabbit	Other	Slightly irritating
5.2.2	Eye Irritation	Rabbit	Other	Slightly irritating
5.3	Skin Sensitisation	Guinea pig	OECD TG 406	Not sensitizing
5.4	Repeated Dose Toxicity	Rat	OECD TG 421	NOAEL = 100 mg/kg bw LOAEL = 300 mg/kg bw
5.5	Genetic Toxicity *In Vitro*			
A.	Bacterial Test	*S.typhimurium, E. coli*	Japanese Guideline and OECD TG 471 & 472	- (With metabolic activation) - (Without metabolic activation)
B.	Non-Bacterial *In Vitro* Test	CHL/IU cells	Japanese Guideline	- (With metabolic activation) - (Without metabolic activation)
5.6	Genetic Toxicity *In Vivo*	Mouse	Other	No valid data
5.7	Carcinogenicity	Mouse	Other	No valid data
5.8	Toxicity to Reproduction	Rat	OECD TG 421 Preliminary toxicity screening test	NOAEL = 100 mg/L (male) NOAEL = 1,000 mg/L (female) NOAEL = 1,000 mg/L (Offspring)
5.9	Developmental Toxicity/ Teratogenicity			None
5.11	Experience with Human Exposure			None

[Note] Data beyond SIDS requirements can be added if the items are relevant to the assessment of the chemical, e.g. corrosiveness/irritation,carcinogenicity.

SIDS Initial Assessment Report
for
13th SIAM
(November 6-9, 2001)

Chemical Name: Tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate

CAS No: 3319-31-1

Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:
Mr. Koji Tomita, Ministry of Foreign Affairs, Japan

HISTORY:
The original IUCLID documents were prepared by European Commission. Dainippon Ink and Chemicals Inc., Japan reviewed the documents after incorporation of Japanese testing results.

COMMENTS:
ICCA Initiative work led by Dainippon Ink and Chemicals Inc., Japan

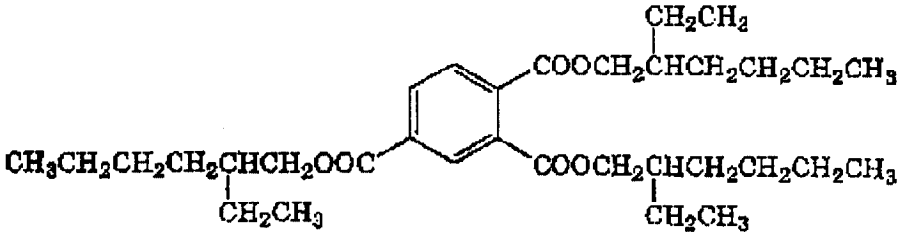
Deadline for circulation:
Date of Circulation:

SIDS INITIAL ASSESSMENT REPORT (SIAR)

Tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate

1. IDENTITY

IUPAC Name: Tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate
CAS Number: 3319-31-1
Molecular formula: $C_{33}H_{54}O_6$ (MW=546.79)
Structural formula:



Synonym: TOTM
Tris(2-ethylhexyl) trimellitate
Benzene-1, 2, 4-tricarboxylic acid tris-(2-ethylhexyl) ester

Purity: >99. 5%

Impurity: Di(2-ethylhexyl) phthalate (DEHP) < 0.1%
Water

Additives: None

Table 1. Physical and Chemical Properties

Items	Protocol	Results
Melting Point	OECD TG 102	< -50°C
Boiling Point	Unknown	283°C(4 hPa)
Density	Unknown	0.987 - 0.990 g/cm³(20°C)
Vapor pressure	OECD TG 104	<2.8 x 10^{-4} Pa(100°C)
Partition Coefficient (LogP_{ow})	OECD TG 107	5.94 (25°C)
Water Solubility	OECD TG 105	0.13 mg/ L (25°C)

2. GENERAL INFORMATION ON EXPOSURE

The production volume of TOTM in Japan is approximately 20,000 tonnes /year and also, there are 5 manufacturers in Japan. Estimated global production is 40,000 – 100,000 tonnes/year. TOTM is produced in closed system and mainly used as plasticizer for PVC electrical cable and wire especially for high temperature application.TOTM is no source of potential release to the environment except for sampling and maintenance of the production facilities.

2.1 Environmental Fate

Based upon the biodegradation measurement, the substance is not readily biodegradable. TOTM achieved 4.2 percent of its theoretical BOD using an activated sludge inoculum during a 4 weeks incubation in a single screening study.

The Mackay levelIII fugacity model was employed to estimate the environmental distribution of TOTM in air, water, soil and sediment. The calculation results are shown in Table 2.If released to air, an estimated vapor pressure of less than 2.8 x 10^{-4} Pa at 100°C indicates TOTM will exist solely in the particulate-phase in the ambient atmosphere. Particulate-phase TOTM is removed from the atmosphere by wet and dry deposition. If released to soil, TOTM isnot expected to have mobility based upon the fugacity model calculation Volatilization from soil surfaces is not expected to be an important environmental fate process based on theestimated vapor pressure of this substance. If released into water, TOTM is expected to adsorb to suspended solids and sediment in water based upon thefugacity model calculation. [Dainippon Ink and Chemicals, Inc. (2001)]
Hydrolysis may be an important environmental fate process based onestimated hydrolysis half-lives of 17.5 and 11.9 days at pH 7 and 9, respectively. Measured BCF values of less than1 to 2.7 in carp suggest that bioconcentration in aquatic organisms is low.

Table 2. Predicted distribution of TOTM using Fugacity level III (%)

Compartment	*Release 100% to air*	*Release 100% to water*	*Release 100% to soil*
Air	19.6	0.0	0.0
Water	4.7	32.7	0.0
Soil	66.2	0.1	100.0
Sediment	9.5	67.2	0.0

2.2 Human Exposure

2.2.1 Occupational exposure

The substance is produced and used in closed system. So, occupational exposure is limited in the case of sampling and maintenance at the production facilities. Moreover, the exposure time is very short. The major rout of occupational exposure is inhalation and dermal.
The atmospheric concentration was measured at two production sites in Japan. The monitoring data are shown in Table 3. The maximum exposure level is estimated according to working schedules as follows. From Table 3, if a single worker (Body weight; 70 kg, respiratory volume; 1.25 m^3/hour) is assigned to implement all daily operation without protection, the daily intake (EHE inh) is calculated as 1.77 x 10^{-3} mg/kg/day as the worst case. On the other hand, a single worker (surface area of exposed skin 840 cm^2 for hands) daily dermal dose (EHE der) is calculated as 2.47 mg/kg/day based on below calculation as the worst case without protection. Workers wear protective gloves and goggles during the operation, sosignificant exposure is not expected.

Table 3. Available workplace monitoring data for TOTM (EHE inh)

Occupation	Frequency Times/day	Duration Hr	Working hr/day	Max concentration mg/m^3	EHE inh mg/kg/day	Reference
Sampling	5	0.017	0.085	0.210	$3.19x10^{-4}$	JISHA, Japan (2001)
Analysis	5	0.067	0.335	0.053	$3.17x10^{-4}$	
Charge to drum	1	0.833	0.833	0.076	$1.13x10^{-3}$	
Total	11	-	1.253	-	$1.77x10^{-3}$	

EHE inh: Estimated Human Exposure for inhalation

Calculation: EHE der = (Cder * T * S * t) /W

EHE der: Estimated Human Exposure for dermal
Cder = 990 mg/cm^3 (Rate in product contacted by worker)
T = 0.01 cm (Thickness of substance)
S = 840 cm^2 (Surface area of exposed skin) for hand
t = 0.0208 day/day (Exposure time per day ; 10min/8Hr, [1day = 8Hr] assumed)
W = 70 Kg (body weight)

2.2.2 Consumer exposure

Usually, this substance has been already blended to the compound asplasticizer, so it is not expected that downstream users or consumers of electric wire industry may expose to this substance.

3.HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics and metabolism

Absorption and metabolism were studied for TOTM(14C-labeled on the 2-carbon atom of 2-ethylhexyl group) mixed with corn oil and administered by gavage in a single dose of 100 mg/kg of body weight in 4 male SDrats. About 75% of the dosewas excreted unchanged in the feces, 16% in the urine as metabolites and 1.9% was expired as $^{14}CO_2$. Radioactivity was excreted in the feces as unchanged TOTM (85% of the fecal radioactivity), mono- and di(2-ethylhexyl)trimellitate(MOTM and DOTM, respectively), and as unidentified polar metabolites. Metabolites in the urine were identified as MOTM and metabolites of 2-ethylhexanol less than 0.6% of the dose remained in the tissues. Elimination of $^{14}CO_2$ was biphasic with half-lives of 4.3 and 31 hrs, and excretion of radioactivity in the urinewas biphasic with half-lives of 3.4 hrs and 42 hrs. [Eastman Kodak Company]

3.1.2 Acute toxicity

Acute toxicity data are mainly reported for rat, mice and rabbits. We could find 12 acute toxicity data for animals(oral(6), inhalation(1), IP(2) and dermal(3)) test data, and one(oral) study (MHW, Japan (1996)) and two(oral and dermal) studies (Nuodex Inc.(1981), Nuodex Inc(1982c)) were conducted by the method of OECD TG and similar method to OECD TG, respectively.
The data, which we feel informative to evaluate the acute toxicity, are listed in Table 4.

Table 4. Summary of effects of TOTM on animals (Acute Toxicity)

Route	Animals	Values	Type	References
Oral	Rat	>2000 mg/kg	LD_{50}	MHW, Japan (1996)
	Rat	>5000 mg/kg bw	LD_0	Nuodex Inc.(1981)
Inhalation	Rat	>2600 mg/m^3	LC_0	Nuodex Inc.(1982b)
Dermal	Rabbit	>2 ml/kg	LD_0	Nuodex Inc(1982c)
	Rabbit	>1970 mg/kg bw	LD_0	Tenneco Chemicals(1981))
I.P.	Rat	>3200 mg/kg bw	LD_{50}	Eastman Kodak (1983)
	Mouse	>3200 mg/kg bw	LD_{50}	Eastman Kodak (1983)

It can be concluded that acute toxicity (Oral) of TOTM is LD_{50} >2000 mg/kg in rat.

3.1.3 Repeated dose toxicity

Among the eight available data, four were conducted under the GLP. Three studies were considered to be key study.

The first study was the oral study by CMA(1985). The subchronic toxicity of TOTM administered orally in the diet togroups of 5 male and 5 femaleFischer 344 rats at levels of 0(0), 0.2(184), 0.67(650), 2.0(1826) % (mg/kg bw/day) for 28 days was determined. There were no statistically significant differences in body weights between control andTOTM treated groups. There was a significant difference between control and treated groups in thefollowing: absolute and relative liver weights (higher in both sexes at all levels except 0 or 0.2%)serum albumin (higher in both sexes at 0.67 or 2.0%), serum cholesterol levels (higher in males at 0.67 or 2.0%). Liver biochemistry revealed statistically significant differences between treated and control groups as indicated by palmitoyl CoA oxidation (increased in both sexes at 20% and males at all dose levels), andcatalase activity (increased inmales at 2.0%). So, the NOAEL for repeated dose toxicity is considered to be 184 mg/kg and the LOAELis 650 mg/kg for both sexes.

The second study was the oral study by MHWJapan(1996). No test substances related changes were noted in terms of clinical signs, body weight, food consumption, and hematology, blood examination, urinalysis, and pathological findings. So, the NOEL for repeat dose toxicity is considered to be 1,000 mg/kg/day for both sexes.

The third study was the OECD preliminary reproduction toxicity screening test by MHW Japan(1998). Gavage study in SD rats conducted at doses of 100, 300 and 1,000 mg/kg/day (Male; 46days, Female; from 14days before mating to day 3 of lactation)of TOTM. The decreases in spermatocytes and spermatids in males was observed for 300 and 1.000 mg/kg groups by histopathological examination. No effects on general appearance, body weight, food consumption, autopsy findings, weights of the reproductive organs ofboth sexes, or histopathlogical features of the ovary were detected. So, the NAOEL is considered to be 100 mg/kg/day for males, and 1,000 mg/kg/day for females.

There is no available information on human toxicity.

Conclusions:

The NOAEL and the LOAEL for repeated oral toxicity are considered to be 100 and 300 mg/kg/day for rats, respectively.

3.1.4 Genotoxicity / Mutagenicity

We can find five reports for Ames Tests. One (MHW, Japan: 1996) is conducted under GLP and others are not. The study of MHW is considered to be a key study.
TOTM has been investigated *in vitro* tests. This substance did not induce gene mutation in bacterial system (MHW, Japan: 1996), and chromosomal aberration in mammalian cultured cells (MHW, Japan: 1996), with and without an exogenous metabolic activation system. Among these studies, MHW study was identified to be a key study because it was well conductedand reported.

Reverse gene mutation assay was conducted by OECD TG 471and 472, using pre-incubation method. TOTM was not mutagenic in*Salmonella typhimurium* TA100, TA1535, TA98, TA1537 and Escherichia coli WP2 uvrA at concentration of up to 5000 ug /plate, with or without an exogenous metabolic activation system (MHW, Japan:1996).

Chromosomal aberration test by OECD TG 473 was conducted in cultured Chinese hamster lung (CHL/IU) cells. Structural chromosomal aberrations and polyploidy were not inducedup to a maximum concentration of 5.0 mg/mL on continuous treatment, and with Short-term treatment, with and without an exogenous metabolic activatin system (MHW, Japan: 1996).

And all other test results (HGPRT assay, Unscheduled DNA synthesis, Dominant Lethal Assay for example) shows that TOTM is not genetoxic

Conclusions:
This substance is considered to be not genotoxic with and without an exogenous metabolic activation system in bacterial test and chromosomal aberration test*in vitro*.

3.1.5 Carcinogenecity

One brief report states only that tests in mice, with a propensity to form pulmonary adenomas, were negative for TOTM, unlike those using urethane. Thecarcinogenecity tests revealed that the chemical is negative but test result was invalid.

3.1.6 Reproduction/developmental toxicity

The OECD Preliminary Reproduction Toxicity Screening Test was performed. [MHW, Japan: 1998]. This study was identified to be well conducted andreported.
Gavage study in SD rats conducted at doses of 100, 300 and 1,000 mg/kg/day (Male; 46days, Female; from 14days before mating to day 3 of lactation)of TOTM.
Histopathological examination of the testes revealed decreases inspermatocytes and spermatids in males of the 300 and 1,000 mg/kg groups. No effects of TOTM were detected on general appearance, body weight, food consumption, autopsy findings, and weight of reproductive organs of both sexes, or on histopathological examination of the ovary. On the basis of these findings, the NOELs of TOTM for repeat dose toxicity are considered to be 100mg/kg/day for males, and 1,000 mg/kg/day for females.
Except for the effects in males observed on histopathological examination, no influence of this substance was detected regarding reproductive ability, organ weights or histopathological appearance of the ovaries, delivery or maternal behaviorof dams. No effect of TOTM were detected on viability, general appearance,body weight or autopsy findings of offspring.On the basis of these findings, theNOELs for reproductive/ developmental toxicitywere considered to be 100mg/kg/day for male rats, 1,000 mg/kg/day for female rats, and 1,000 mg/kg/day for offspring.

Conclusions:

The NOELs for reproductive/developmental toxicity were considered to be 100 mg/kg/day for male rats, 1,000 mg/kg/day for female rats, and 1,000 mg/kg/day for offspring, respectively.

3.1.8 Other : Irritation and sensitization

Six and three results are reported for skin and eye irritation test, respectively. All these test results showed that TOTM is slightly irritating to the skin and the eye.

Sensitization test on guinea pig using OECD/TG 406 (Tenneco Chemicals, 1981) showed " no sensitization".

3.2 Initial Assessment for Human Health

Acute toxicity of TOTM is considered to be LD_{50} >2000 mg/kg in rat.
In the irritation-test for animals, TOTM is slightly irritating to the skin and the eye.
Sensitization test on guinea pig using OECD/TG 406 showed " no sensitization".
The NOAEL and the LOAEL for repeated oral toxicity are considered to be 100 and 300 mg/kg/day for rats, respectively
The NOELs for reproductive/developmental toxicity were considered to be 100 mg/kg/day for male rats, 1,000 mg/kg/day for female rats, and 1,000 mg/kg/day for offspring, respectively.
This substance is not genotoxic with and without an exogenous metabolic activation system in bacterial test and chromosomal aberration test *in vitro*.

TOTM produces the same spectrum of morphological and biochemical change in the rat liver as DEHP. TOTM, however, was much less potent in its action, with a dietary level of 2.0%, causing less peroxisome proliferation and peroxisome-associated enzyme induction than 0.67% DEHP. Also, the level of peroxisome induction in rats given TOTM is less than in those receiving a metabolically equivalent dose of 2-ethylhexanol. Furthermore, on a molar basis, effects were lower than with DEHP. An effect of MEHP, a metabolite of DEHP, was not seen with TOTM. [The British Industrial biological Research Association (1985), EPA OTS0510637(1985), JOHN R. HODGSON. (1987)]

In addition, recently studies have determined that rodents (rats) are susceptible to peroxisome proliferation. After all, these results suggest that the effect of DEHP on liver are markedly different between other species (marmosets) and rodents (rats). Yoshimasa Kurata et al. (1998)] Therefore, DEHP was downgraded from Group 2B to Group 3 by the IARC Monographs Working Group. (February 2000) Group 3 is " cannot be classified as to its carcinogenicity to humans".

4. Hazards to the Environment

4.1 Aquatic Effects

TOTM has to be considered as weakly toxic against aquatic organisms. Aquatic effects were tested and results are summarized in Table 5. As the lowest acute and chronic toxicity data, EC_{50} (>100 mg/L ,72hr) of *Selenastrum capricornutum* ATCC22662 and NOEC (55.6 mg/L, 21day) of Daphnia magna were adopted, respectively.

Table 5. Summary of effects of TOTM on aquatic organisms

Organism	Test duration	Result (mg/L)	Reference
Algae			
Selenastrum capricornutum ATCC22662	72 hr	EC_{50} >100 NOEC>100	EA, Japan
Invertebrates			
Daphnia magna	24 hr	EC_{50} >180	EA, Japan
	48 hr	EC_{50} >180 NOEC>180	
	48hr	EC_{50} >1	ICI 1990
	21 day	EC_{50} =89.1 NOEC=55.6	EA, Japan

	21 day	NOEC=0.082	CMA (1985)
Fish			
Oryzias latipes	96 hr	LC_{50} >100	EA, Japan
	14 day	LC_{50} >75 NOEC>75	EA, Japan

As the acute toxicity data, EC_{50} (>100 mg/L ,72hr) of *Selenastrum capricornutum* ATCC22662 and EC_{50} (180 mg/L, 48hr) of Daphnia magna were adopted, respectively. As the chronic toxicity data of Daphnia magna and the prolonged toxicity data of fish (Oryzias latipes), NOEC =0.082mg/L (21days) [CMA; 1985] and NOEC=75mg/L (14days) [EA Japan] were adopted, respectively. All those data in supersaturated solution, which was considered to be homogeneous substantially, was obtained with the aid of solubilizer (HCO-40). Though the observed concentration data was less reliable, one chronic toxicity data (NOEC >0.082mg/L) was reported in a lower concentration than saturation point.

Two other acute (ICI 1990) and chronic(EA Japan) data would be helpful for evaluation of the toxicity for Daphnia magna. These tests were conducted in a supersaturated solution.

Assessment factor of 100 was chosen to determine the lowest PNEC. Thus, calculated PNEC (=0.00082 mg/L) of TOTM is closely to the value of one hundredths (assessment factor) of saturation point. From these toxicity data, it is difficult to decide the exact PNEC, but we are sure that TOTM is practically non-toxic against aquatic organisms.

4.2 Terrestrial effects

There is no available information.

4.3 Initial assessment for the Environment

Hydrolysis may be an important environmental fate process based onestimated hydrolysis half-lives of 17.5 and 11.9 days at pH 7 and 9, respectively. The substance is not readily biodegradable. Measured BCF values of this chemical is reported as less than 1 to 2.7 in carp for 6 weeks, which suggest that bioconcentration in aquatic organisms is much lower than the value eatimated from logPow(=5.94). If released into surface water water, TOTM is expected to adsorb to suspended solids and sediment based upon the fugacity model calculation. The sediment toxicity data was not available, and will need to assess when obtained.

5. Conclusions and recommendations

5.1 Conclusions

Exposure (Physical/chemical property, production, use and distribution)
TOTM is manufactured as the plasticizer of PVC application.
The production volume of TOTM in Japan isapproximately 20,000 tonnes /year and also, there are 5 manufacturers in Japan. Estimated global production is 40,000 – 100,000 tonnes/year. TOTM is produced in closed system andmainly used as plasticizer for PVC electrical cable and wire. And so, this substance has been already blended to the compound asplasticizer, so it is not expected that downstream users or consumers of electric wire industry may expose to this substance.

Occupational exposure may occur through dermal contact and inhalation of vapor. The process

is constructed by closed system and workers wear protective gloves and goggles during the operation, so significant exposure is not expected.
In case of disposal, this substance would be incinerated with following all regulations. Therefore, it is not significant released to theenvironment

Human health
Acute toxicity of TOTM is low, LD_{50} >2,000 mg/kg in rats. In the irritation-test for animals, this substance is slightly irritating to the skin and the eyes. Sensitization test on guinea pig showed "no sensitization". Oral study in rats conducted for 28 days at doses of0(0), 0.2(184), 0.67(650), 2.0(1826) % (mg/kg bw/day) of TOTM. There were no statistically significant differences in body weights between control andTOTM treated groups. There was a significant difference between control and treated groups in thefollowing: hemoglobin concentration (lower in both sexes, 0.67 or 2.0% TOTM), leucocyte counts (higher in males at 0.67 or 2.0%), absolute and relative liver weights (higher in both sexes at all levels except 0 or 0.2%),serum albumin (higher in both sexes at 0.67 or 2.0%), serum cholesterol levels (higher in males at 0.67 or 2.0%), serum urea (higher in males at 2.0%), serum lipids (decreased in females a0.2%). Liver biochemistry revealed statistically significant differences between treated and control groupsas indicated by palmitoyl CoA oxidation (increased in both sexes at 20% and males at all dose levels), and catalase activity (increased in males at 2.0%). Therefore, the NOAEL and the LOAEL for repeated oral toxicity were considered to bc100 and 300 mg/kg/day for male rats.
The NOELs for reproductive/developmental toxicity were considered to be>1,000 mg/kg/day for female rats and for offspring.
TOTM is not genetoxic/mutagenic in bacterial and mammalian cell tests *in vitro* tests. The carcinogenecity tests revealed that the chemical is negative but test result was invalid.

Environment
The Mackay levelIII fugacity model was employed to estimate the environmental distribution of TOTM in air, water, soil and sediment. If released to air, TOTM will exist solely in the particulate-phase in the ambient atmosphere. If released to soil, TOTM is not expected to have mobility. If released into water, TOTM is expected to adsorb to suspended solids and sediment in water.
Measured BCF of values of less than 1 to 2.7 in carp suggest that bioconcentration in aquatic organisms is low.

As the lowest acute and chronic toxicity data, EC_{50} (>100 mg/L, 72hr) of *Seletiastrum capricornutum* ATCC22662 and NOEC (0.082mg/L, 21day) of Daphnia magna were adopted, respectively. Assessment factor of 100 was chosen to both acute and chronic toxicity data to determine PNEC Thus, PNEC of TOTM is 0.00082mg/L.

5.2 Recommendations
The chemical is currently of low priority for further work.

6. References
Chemicals Evaluation and Research Institute, Japan Ministry of International Trade and Industry (1998)

Chemicals Inspection and Testing Institute Japan.Chemical Industry Ecology-Toxicology and Information Center. (1992)

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Yoshimasa Kurata. Subchronic Toxicity of Di(2-ethylhexyl)phthalate in Common Marmosets: Lack of Hepatic Peroxisome Proliferation, Testicular Atrophy, or Pancreatic Acinar Cell Hyperplasia. Toxicological Sciences 42, 49-56 (1998)

PROPOSED ROBUST SUMMARY for Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate

CAS No. 3319-31-1

Sponsor country: Japan

Date: Aug 24, 2001

PHYSICAL/CHEMICAL ELEMENTS

MELTING POINT

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 102
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** Not stated.

RESULTS

- **Melting point value:** <-50 °C (223 K)
- **Decomposition:** Not stated.
- **Sublimation:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Melting point is <-50°C (223 K).

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BOILING POINT (a)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Boiling point value:** 283°C
- **Pressure:** 4
- **Pressure unit:** hPa
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Boiling point is283°C at 4 hPa.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES

Midwest Research Institute; Thomas W. Lapp, Charles EMumma Joseph Chaszar: A Survey of Plasticizers: Epoxies, Linear Polyesters andTrimellitates Chemical Technology and Economics in Environmental Perspective, Task IV, Environmental Protection Agency (Nov. 1981)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BOILING POINT (b)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Boiling point value:** 414°C (687K)
- **Pressure:** 1,013
- **Pressure unit:** hPa
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Boiling point is414°C at 1,013hPa.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** The Sigma-Aldrich Library of Regulatory and Safety Data.

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

DENSITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method:** Not specified.
- **GLP:** Not stated.
- **Year:** Not stated.
- **Remarks:** Not stated.

RESULTS

- **Density:** 0.987 – 0.990 g/cm^3
- **Temperature** 20°C
- **Remarks:** Not stated.

CONCLUSIONS

Density is 0.987-0.990 g/cm^3 at 20°C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES

Midwest Research Institute; Thomas W. Lapp, Charles EMumma Joseph Chaszar: A Survey of Plasticizers: Epoxies, Linear Polyesters andTrimellitates Chemical Technology and Economics in EnvironmentalPerspective, Task IV, Environmental Protection Agency (Nov. 1981)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

VAPOR PRESSURE (a)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 104
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** Not stated.

RESULTS

- **Vapour Pressure value:** $< 2.8 \times 10^{-4}$ Pa
- **Temperature:** 100 °C
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Vapour pressure is $< 2.8 \times 10^{-4}$ Pa at 100 °C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

VAPOR PRESSURE (b)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable.

METHOD

- **Method/guideline:** Not stated
- **GLP:** Not stated
- **Year:** Not stated
- **Remarks:** Not stated.

RESULTS

- **Vapour Pressure value:** 0.27 – 6.7 hPa
- **Temperature:** 250 – 260 °C
- **Decomposition:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

Vapour pressure is 0.27- 6.7 hPa at 250 – 260 °C.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Not stated.

REFERENCES

Midwest Research Institute; Thomas W. Lapp, Charles E Mumma Joseph Chaszar: A Survey of Plasticizers: Epoxies, Linear Polyesters and Trimellitates Chemical Technology and Economics in Environmental Perspective, Task IV, Environmental Protection Agency (Nov. 1981)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

PARTITION COEFFICIENT

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene 1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 107 (Shake Flask Method, 1995)
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** Not stated.

RESULTS

- **Log P_{ow} :** 5.94
- **Temperature:** 25°C ±1°C
- **Remarks:** Test condition: Test was conducted in duplicate under the following three conditions. Test chemical was analyzedby HPLC.

Test condition	Condition-1	Condition-2	Condition-3
1-Octanol saturated with water	10 mL	20 mL	40 mL
Water saturated with 1-octanol	240 mL	230 mL	210 mL
Test chemical in 1-octanol saturated with water (52.2 mg)	10 mL	10 mL	10 mL

Test results	Log Pow		
	a	b	Mean
Condition-1	5.99	5.99	
Condition-2	5.95	5.87	5.94
Condition-3	5.92	5.93	

CONCLUSIONS log P_{ow} is 5.94.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**

Remarks:

WATER SOLUBILITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method:** OECD TG 105 (flask method).
- **GLP:** Yes
- **Year:** 1998.
- **Remarks:** Not stated.

RESULTS

- **Value:** 0.13 mg/L at 25 °C±1°C
- **Description of solubility:** Of very low solubility
- **pH value:** No dissociation group.
- **pKa value:** There is no pertinent functional group.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is very low solubility in water.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS

STABILITY IN WATER

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: 98.5%

METHOD

- **Method/guideline:** OECD TG 111
- **Type :** Hydrolysis as a function of pH
- **GLP:** Yes
- **Year:** 1998
- **Remarks:** No hydrolysis of test chemical was observed at pH 4 at 50°C±1°C for 5 days. Hydrolysis rates at pH 7 were determined at 60, 70 and 80 °C, and at pH 9 at 50, 60, and 70 °C . They were extrapolated to 25 °C using Arrhenius relationship. Half life at 25 °C was calculated from the rate constant.

RESULTS

- **Nominal:** ca. 0.2 mg/L
- **Measured value:** Not stated.
- **Degradation:** No hydrolysis occurred in 5 days, at 50 °C pH 4. At pH 7 and pH 9, test chemicals were hydrolysed at all temperatures studied.
- **Half-life ($t_{1/2}$):**

	Rate Constant (hr^{-1})	Half-life(day)
pH 7	1.66×10^{-3}	17.5
pH 9	2.44×10^{-3}	11.9

- **Breakdown products:** Not stated.
- **Remarks:** Not stated.

CONCLUSIONS

This chemical is stable in aqueous water at pH 4 under the condition studied, but it ishydrolysed at pH 7 and pH 9 at 25 °C with half-life of 17.5 and 11.9 days.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemicals Evaluation and Research Institute (Kurume, Japan).

REFERENCES

Ministry of International Trade and Industry (1998)

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Not applicable.

METHOD

- **Test:** Calculation
- **Method:** Fugacity level III
- **Year:** 2001
- **Remarks:** The parameters used are shown in Appendix.

RESULTS

- **Media :**
- **Estimated Distribution under three emissionscenarios:**

Compartment	Release100 % to air	Release 100 % to water	Release 100 % to soil
Air	19.6 %	0.0 %	0.0 %
Water	4.7 %	32.7 %	0.0 %
Soil	66.2 %	0.1 %	100.0 %
Sediment	9.5 %	67.2 %	0.0 %

- **Remarks:**

CONCLUSIONS

If this chemical is released into water the majority of this chemical is expected to stay in sediment, but if it is released into air or soil, this chemical is expected to stay in soil

DATA QUALITY

- **Reliabilities:** Key study.
- **Remarks:** Not stated.

REFERENCES

Dainippon Ink and Chemicals, Incorporated (2001), unpublished report.

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BIODEGRADATION

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Unavailable

METHOD

• **Method:**	OECD TG 302C "Inherent Biodegradability: Modified MITI Test(II)"
• **Test Type:**	Aerobic
• **GLP:**	No
• **Year:**	1977
• **Contact time:**	28 days
• **Inoculum:**	The supernatant (500ml) of activated sewage sludge obtained from ten sampling sites and 5 liters of supernatant removed from a previously established culture are transferred to a culture vessel. The pH of the culture mixture was adjusted to 7.0±1.0 and constantly aerated . Thirty minutes after stopping aeration, discard about 1/3 of the whole volume of the supernatant, and add an equal volume of 0.1% synthetic sewage and the aeration re-started. Repeat this procedure once a day.
• **Remarks:**	During the aeration, appearance of supernatant and the formation of activated sewage was observed. The sludge was found to form a clear supernatant on settling and formed cloudyflocs when on aeration. Operating temperature, pH and a dissolved oxygen concentration were recorded. The protozoa of sludge were observed under an optical microscope. *Incubation apparatus: Respirometry(Closed bottle) Ohkura Electric Co. *CO2 absorbent: Soda lime No.1 (Wako pure chemicals Inc.) *Stirrer : Magnetic stirrer *Temperature : 25±1℃ *Concentration of test chemical: 30mg/L, 100mg/L *Reference substance: Aniline

RESULTS

• **Degradation:**	
• **Results:**	4.2% after 28days
• **Kinetic:**	The percentage degradation in term of oxygen consumption was calculated as follows: % degradation = (BOD-B)/TOD x 100 BOD: Biological Oxygen Demand of the test material B : Oxygen consumption in basal culture medium to which inoculum is added (control) TOD: Theoretical oxygen demand to completely oxidize the test Material
• **Breakdown products:**	Not stated.

- **Remarks:** At the end of incubation, measure the residual dissolved organic carbon and test material concentration. The reference substance, aniline attained more than 40% and 60% degradation after 7 and 14days confirming the suitability of the inoculum and culture conditions.

CONCLUSIONS

This chemical is low biodegradable.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out by Chemical Inspection and Testing Institute.

REFERENCES

Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan(1992)

Ministry of International Trade and Industry

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

BIOACCUMULATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Unavailable

METHOD

- **Method:** OECD TG 305C
- **Species:** *Cyprinus Carpio* (Obtained from Nakajima hatchery in Kumamoto, Japan)
- **GLP:** No
- **Year:** 1978
- **Exposure Period:** 42 days
- **Remarks:**

Test fish: Acclimated for ca. 8 weeksbefore testing at 25±2℃. Fish with ca.10cm in length and ca.30g in weight were selected at random. Lipid content was 2-6%.

Test condition: Concentrations: 0.2 and 2 mg/L, solubilizer controlled
Type of test: flow-through (200-800mL/min), 100L glass tank.
Dissolved oxygen concentration: 6-8mg/L
Temperature: 25 ±2℃
Water chemistry was tested in the control and two concentrations every 2 times in a week.
Test was conducted in duplicate every 2 weeks for two concentrations (The control was done before and after testing.)

RESULTS

- **Results:** BCF=1-2.7 (concentration: 0.2mg/L)
  BCF=0.1-0.23(concentration: 2mg/L)
- **Kinetic:** BCF=C1/C2
  C1: Concentration of this chemical in Fish
  C2: Concentration of this chemical in water
- **Breakdown products:** Not stated.

CONCLUSIONS

This chemical is low bioaccumulation.

DATA QUALITY

- **Reliabilities:** Key study
- **Remarks:** Well conducted study, carried out byChemical Inspection and Testing Institute

REFERENCES

Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan(1992)

Ministry of International Trade and Industry

OTHER

- **Last changed:**
- **Order number for sorting**
- **Remarks:**

ECOTOXICITY ELEMENTS

ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method:** OECD TG 203
- **Type:** Semi-static
- **GLP:** Yes
- **Year:** 1998.
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka): Obtained from commercial domestic hatcheries.
- **Analytical monitoring** Yes. Test solutions were measured byHPLC before and after 24 hours exposure period. Test solutions were replaced every 24 hours to new ones.
- **Exposure period (h):** 96
- **Statistical methods:** Not applicable because of nomortality.
- **Remarks:**

Test fish: Acclimated for more than 12 days before testing; any groups showing no mortality for 7 days before test started. Fish with 22.1 mm (18.3–23.8 mm) in length were selected at random. Average body weight of fishwas 0.1462g (n=10).

Test conditions: Details of test: Semi-static (water changedevery 24 hours)
Dilution water source: Tap water after dechlorinated by passing through activated carbon.
Dilution water chemistry: Hardness: 25 mg/L as $CaCO_3$; pH: 6.7
Stock and test solution and how they are prepared: Pipette or pour the appropriate amount of the solution (0.3 wt% of test chemical/with solubilizer hydrogenated caster oil HCO-40 3000mg/l) into the test waters.
Concentrations dosing rate, flow-through rate, in what medium: Concentrations of 0, 100 mg/L and dispersant control weretested.
Vehicle/solvent and concentrations: Hydrogenated caster oil HCO-40, 100mg/L
Stability of the test chemical solutions: Stable, measured concentration was 101-103%.
Exposure vessel type: 10 fish per group in 3L glass beaker without acration under room light
Number of replicates, fish per replicate: One replicatewas done.
Water chemistry in test (O_2, pH) in the control and all concentration where effects were observed: Dissolved oxygen readings and pH values were taken daily during 96 h exposure period.
Dissolved oxygen concentration: 5.0–9.2 mg/L.

pH values: 6.7-6.8.
Test temperature range:Water temperature at 23.5-24.1°C.
Method of calculating mean measured concentrations: Geometric mean.

RESULTS

- **Nominal concentrations:** 0, 100 (mg/L)
- **Measured concentrations:** <1, 103 (0hr), <1, 102 (24hr)
- **Unit:** mg/L.
- **Element value** LC_{50} at 96 hours >100.0 mg/L based on nominal concentrations.
- **Statistical results as appropriate:**Not applied.
- **Remarks field for Results:**

Biological observations Not described.
Table showing cumulative mortality:

Percent mortality of *Oryzias latipes* exposed to the test chemical

Nominal concentration (mg/L)	Cumulative number of dead fish (% mortality)			
	24 hour	48 hour	72 hour	96 hour
Control	0(0)	0(0)	0(0)	1(10)
Dispersant Control	0(0)	0(0)	0(0)	0(0)
100	0(0)	1(10)	1(10)	1(10)

Lowest test substance concentration causing 100% mortality:
Not obtained under the test conditions studied.
Mortality of controls: 1 fish was dead at 96h.
Abnormal responses: At 24 hr, one fish showed abnormal breathing behaviour at 100mg/L.
Reference substances: Copper(II)sulfate pentahydrate. LC_{50} at 96h was 0.43 mg/L.
Any observations, such as precipitation that might cause a difference between measured and nominal values: It became clouded in 100mg/L concentration, but not precipitation.

CONCLUSIONS

LC50 (96h) > 100mg/L for fish.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
- Experimental design and analytical procedure were well documented.
Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed:**
- **Order number for sorting:**

- **Remarks field for GeneralRemarks:**

PROLONGED TOXICITY TO FISH

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method:** OECD TG 204
- **Type:** Flow-through.
- **GLP:** Yes.
- **Year :** 1998.
- **Species/Strain/Supplier:** *Oryzias latipes* (Medaka): Obtained from commercial domestic hatcheries.
- **Analytical monitoring:** Yes. Test solutions were measured byHPLC before and after 7, 14days exposure period.
- **Exposure period:** 14 day.
- **Statistical methods** Binomial method (TOXDAT MULTI-METHOD PROGRAM, USEPA)
  Dunnet method was used for LC_{50} and for fish body weight difference, respectively.
- **Remarks field for Test Conditions:**

Test fish: Acclimated for more than 12 days before testing; any groups showing2.9% mortality for 7 days before test started. Fish with 20.0 mm (18.5–21.6 mm) in length were selected at random. Average body weight of fish was 0.484g (0.1182–0.2014g)(n=10). Fish were starved for 24 hours before the test started.

Test conditions: Details of test: Flow-through.
Dilution water source: Tap water after dechlorinated by passing through activated carbon.
Dilution water chemistry: Hardness: 15.3mg/L as $CaCO_3$; pH: 7.0
Stock and test solution and how they are prepared: The working solution (4.8wt% of test chemical with solibilizer HCO-40 controlled) was prepared with the dilution water. The test solution was supplied continuously by mixing the working solution and the dilution water with the help of a mechanically operated quantitative water-pump.
Concentrations dosing rate, flow-through rate, in what medium: Nominal concentrations of 0, 18.8, 37.5 and 75.0 mg/L and Dispersant control were tested.
Vehicle/solvent and concentrationsHydrogenated caster oil HCO-40, Max. 75.0 mg/L
Stability of the test chemical solutions: It became clouded in high concentration, but not precipitation.
Exposure vessel type: 10 fish per group in 3L glass beaker without aeration under room light
Number of replicates, fish per replicate: One replicate was done.
Water chemistry in test (O_2, pH) in the control and one concentration where

effects were observed: Dissolved oxygen readings and pH values were taken every 3 days during the exposure period.
Dissolved oxygen concentration: 6.6~7.7 mg/L.
pH values: 6.9~7.2.

Test temperature range: Water temperature at 23.5~24.1°C (24±2°C).

Method of calculating mean measured:Geometric mean.

RESULTS

- **Nominal concentrations :**0, 18.8, 37.5, 75.0 (mg/L) and dispersant control
- **Measured concentrations :**

Measured concentration of the test chemical during a 14-day exposure of orange killifish (*Oryzias latipes*) under flow-through test conditions

Nominal concentration (mg/L)	Measured concentration (mg/L) (percent of nominal)			
	0 day	7 day	14 day	Mean
Control	< 1.0	< 1.0	< 1.0	--
Dispersant Control	< 1.0	< 1.0	< 1.0	--
18.8	17.7(94.1)	15.8(84.0)	15.5(82.4)	16.3(86.9)
37.5	35.7(95.2)	33.2(88.5)	30.0(80.0)	33.3(87.9)
75.0	70.6(94.1)	68.8(91.7)	71.2(94.9)	70.2(93.6)

- **Unit :** mg/L
- **Element value:**

LC_{50} (7 days) > 75.0mg/L (nominal concentration)
LC_{50} (14 days) > 75.0mg/L (nominal concentration)
NOEC (14 days) > 75.0 mg/L (nominal concentration)

- **Statistical results, as appropriate:**

The mean body weight of fish exposed toall concentration of the test chemical was not significantly different from controls during the test period(1fa=0.05, Dunnet).

- **Remarks field for Results:**

Biological observations: Not described.

Cumulative mortality:

Percent mortality of *Oryzias latipes* exposed to the test chemical under flow-through test Conditions

Nominal conc. (mg/L)	Cumulative number of dead fish (% mortality)														(days)
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Control	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(10)	1(10)	1(10)
Disp. Cont.	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
18.8	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
37.5	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
75.0	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)

Fish weight:

Nominal conc. (mg/L)	Fish weight (g)										
	No.1	No.2	No. 3	No.4	No.5	No.6	No.7	No.8	No.9	No.10	Ave.
Control	0.1879	0.2526	0.1273	0.2239	0.1139	0.1434	0.1708	0.1789	0.1558	-a	0.1727
Disp. Cont.	0.2205	0.1827	0.1192	0.1884	0.1438	0.1823	0.1563	0.2120	0.1635	0.1580	0.1727
18.8	0.1731	0.1513	0.1593	0.1472	0.2150	0.1548	0.1547	0.1306	0.2104	0.1020	0.1598
37.5	0.1264	0.1495	0.1872	0.1237	0.2055	0.1396	0.1805	0.2101	0.1577	0.1303	0.1611
75.0	0.1746	0.1848	0.1804	0.1625	0.1494	0.1633	0.2103	0.1454	0.1600	0.1818	0.1713

- a : No measurement was made because the Orange Killifish was dead.

Lowest test substance concentration causing 100% mortality>75.0 mg/mL (nominal).

Mortality of controls:10 % mortality observed during the test period (12 through 14 days).
Food intake: Fish was fed with TetraMin® fish food (2% of fish body weight).
Abnormal responses: No abnormal response showed through 14 days.
Reference substances (if used)– results: Copper (II) sulfate pentahydrate. LC_{50} at 96h was 0.30 mg/L.
Any observations, such as precipitation that might cause a difference between measured and nominal values: It became clouded high concentration, butnot precipitation.

CONCLUSIONS

LC_{50} (7 days) > 75.0mg/L (nominal concentration)
LC_{50} (14 days) > 75.0mg/L (nominal concentration)
NOEC (14 days) > 75.0 mg/L (nominal concentration)

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed :**
- **Order number forsorting :**
- **Remarks field for GeneralRemarks :**

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (e.g., *Daphnia*)

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01 Purity: >95.0%

METHOD

• **Method:**	OECD TG 202
• **Type:**	Static
• **GLP :**	Yes
• **Year :**	1998
• **Species/Strain/Supplier:**	*Daphnia magna*
• **Analytical monitoring**	Yes. Test solutions were measured byHPLC before and after 48 hours exposure period.
• **Exposure period (h):**	48
• **Statistical methods:**	Not applicable.

Remarks field for Test Conditions:

Test organisms:	Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan). Age at study initiation: Juveniles within 24h old. Control group: Yes.
Test conditions	Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1800mg/L(with solubilizer HCO-40 1000mg/L controlled) with diluting water (Elendt M4) before use.
Test temperature range:	19.9-20.2 °C (average temperature 20°C). Exposure vessel type: 100mL test solution in a 100 mL glass beaker; 4 beakers per treatment Dilution water source: Elendt M4(OECD guideline No.211 Annex 2) Dilution water chemistry: Hardness: 228mg/L as $CaCO_3$ Lighting: room light 16h:8h light-darkness cycle Water chemistry in test: DO= 8.0-8.6mg/L; pH=7.3-7.8. Feeding: none
Test design:	Number of replicates=20 Concentrations: 0, 17.1, 30.9, 55.6, 100 and 180 mg/L, because 48h-EiC_{50} for parent Daphnia (Acute immobilization test) was>1000mg/L. Dispersant control was also tested.
Method of calculating mean measured concentrations	Geometric mean.
Exposure period:	48 h
Analytical monitoring:	By HPLC analysis. 95.1-99.6% of the nominal concentration at preparation; 90.1-97.7% after 48hr.

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (e.g., *Daphnia*)

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01 Purity: >95.0%

METHOD

• **Method:**	OECD TG 202
• **Type:**	Static
• **GLP :**	Yes
• **Year :**	1998
• **Species/Strain/Supplier:**	*Daphnia magna*
• **Analytical monitoring**	Yes. Test solutions were measured byHPLC before and after 48 hours exposure period.
• **Exposure period (h):**	48
• **Statistical methods:**	Not applicable.

Remarks field for Test Conditions:

Test organisms:	Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan). Age at study initiation: Juveniles within 24h old. Control group: Yes.
Test conditions	Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1800mg/L(with solubilizer HCO-40 1000mg/L controlled) with diluting water (Elendt M4) before use.
Test temperature range:	19.9-20.2 °C (average temperature 20°C). Exposure vessel type: 100mL test solution in a 100 mL glass beaker; 4 beakers per treatment Dilution water source: Elendt M4(OECD guideline No.211 Annex 2) Dilution water chemistry: Hardness: 228mg/L as $CaCO_3$ Lighting: room light 16h:8h light-darkness cycle Water chemistry in test: DO= 8.0-8.6mg/L; pH=7.3-7.8. Feeding: none
Test design:	Number of replicates=20 Concentrations: 0, 17.1, 30.9, 55.6, 100 and 180 mg/L, because 48h-EiC_{50} for parent Daphnia (Acute immobilization test) was>1000mg/L. Dispersant control was also tested.
Method of calculating mean measured concentrations:	Geometric mean.
Exposure period:	48 h
Analytical monitoring:	By HPLC analysis. 95.1-99.6% of the nominal concentration at preparation; 90.1-97.7% after 48hr.

RESULTS

- **Nominal concentrations:** 17.1, 30.9, 55.6, 100.0, 180.0 (mg/L) (Solubilizer controlled)
- **Measured concentrations :**

Measure Concentrations of test chemicals during a 48hr.

Nominal Concentration	Measured concentration(mg/L)			Percent of nominal	
(mg/L)	0hr	48hr	Mean	0hr	48hr
Control	< 1.0	< 1.0	-	-	-
Disp.Cont.	< 1.0	< 1.0	-	-	-
17.1	16.3	15.4	15.8	95.3	90.1
30.9	29.4	28.5	28.9	95.1	92.2
55.6	53.0	52.1	52.5	95.3	93.7
100.0	98.4	96.3	97.3	98.4	96.3
180.0	179.2	175.8	177.5	99.6	97.7

- **Unit :** mg/L.
- **Element value** EC_{50} at 24 hours >180.0 mg/L
  EC_{50} at 48 hours >180.0 mg/L
  NOEC > 180.0 mg/L
  LOEC > 180.0 mg/L
- **Statistical results as appropriate:** Not applied.
- **Remarks field for Results:**

Biological observations: Not described.

Table showing mortality or immobility

Mortality or immobility of *Daphnia magna* to the test chemical

Nominal concentration (mg/L)	Cumulative number of dead or immobilized *Daphnia* (Percent Mortality or Immobility)	
	24 hour	48 hour
Control	0(0)	0(0)
Dissolvant Control	0(0)	1(5)
17.1	0(0)	1(5)
30.9	0(0)	0(0)
55.6	0(0)	0(0)
100.0	0(0)	0(0)
180.0	0(0)	0(0)

Lowest test substance concentration causing 100% mortality: Not obtained under the test conditions studied.

Mortality of controls: No mortality observed during test period.

Abnormal responses: No abnormal responses observed during test period

Reference substances: Potassium dichromate EC_{50} at 48h was 0.87 mg/L.

Any observations, such as precipitation that might cause a difference between measured and nominal values: It became clouded in high concentration, but not precipitation.

CONCLUSIONS

EC_{50} (48h) > 180mg/L and NOEC (48h) > 180mg/L for *Daphnia magna*.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed:**
- **Order number forsorting:**
- **Remarks field for GeneralRemarks:**

TOXICITY TO AQUATIC PLANTS (E.G., *ALGAE*)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01
  Purity: >95.0%

METHOD

- **Method/guideline followed :** OECD TG 201
- **Test type :** Static.
- **GLP :** Yes
- **Year :** 1998
- **Species/strain # and source:** *Selenastrum capricornutum* ATCC22662 (purchased from ATCC)
- **Element basis:** Area under the growth curve.
- **Exposure period:** 72 h.
- **Analytical monitoring:** Yes, measured by HPLC at start and end of the test (72hr).
- **Statistical methods:** Bartlett test for homogeneity in variances and One-wayAnova (EcoTox-Statistics Ver.1.0 beta-edition R1.4) were used for EC_{50}, LC_{50} and NOEC determination (p=0.05).

Remarks field for Test Conditions :

Test organisms	Laboratory culture: OECD medium Method of cultivation: Shaking at 100rpm Controls: OECD medium. EC_{50} of potassium dichromate was 0.41 mg/L.
Test Conditions	Test temperature range: 23±2 °C Growth/test medium: OECD medium. Shaking: 100 rpm Dilution water source: OECD medium. Exposure vessel type: 100 mL OECD medium in a 300 mL Erlenmeyer flask with a silicon cap which allows ventilation. Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): pH=7.3-7.4 at start and 8.3-8.8 at end of the test (72 h). Stock solutions preparation: No stock solution was prepared. Test chemical was diluted to100mg/L (solubilizer, HCO-40 100mg/L)with OECD medium and sterilised with filter before use. Light levels and quality during exposure: 4,756-4,822 lux, continuous illumination.
Test design	Number of replicates: Triplicate Concentrations: 0, 100 mg/L and dispersant control were tested. Initial cell number in cells/mL: $1x10^4$

Method of calculating mean measured concentrations:Geometric mean.

RESULTS

- **Nominal concentrations:**
  0, 100 (mg/L) and dispersant control.
- **Measured concentrations :**
  At start of the test (0 hr), <1.0, 80.6, <1.0(mg/L)
  At end of the test (72 hr), <1.0, 68.7, <1.0 (mg/L)
- **Unit :** mg/L
- **Results:** (calculated based on nominal concentrations)
  (1) **Growth inhibition (comparison of area under growth curve)**
  EC_{50} (0-72 h) > 100 mg/L
  NOEC (0-72 h)> 100 mg/L
  (2) **Growth inhibition (comparison of growth rates)**
  EC_{50} (24-48) > 100 mg/L
  EC_{50} (24-72) > 100 mg/L
  NOEC (24-72) > 100 mg/L
- **Was control response satisfactory:**
  Yes: Mean cell density increased to $270x10^6$ cells/mL (270-fold increase) after 72 hr for control. Mean cell density increased to $275x10^6$ cells/mL (275-fold increase) after 72 hr for Dispersant control.
- **Statistical results as appropriate:**
  Significant difference in the growth curve was not observed between values at 100 mg/L and in each control.

Remarks field for Results:

– Biological observations

Cell density at each flask at each measuring point:

Nominal Concentration (mg/L)	Cell Density ($x10^4$ cells/mL)			
	0 hr	24 hr	48 hr	72 hr
Control	1.0±0.00	6.5±0.50	50.5± 3.48	270.5±23.50
Dispersant Control	1.0±0.00	9.3±1.66	57.5± 9.39	275.2±17.22
100	1.0±0.00	16.1±7.82	65.1±12.82	283.3± 7.98

(Each value represents the mean of three sample counts.)

Growth curves: Logarithmic growth until end of the test (72 h).
Percent biomass/growth rate inhibition per concentration: Not described.
Observations: Test group(100mg/L) showed normal and similargrowth to that of control (283 fold increase after 72 hr).

CONCLUSIONS

(1)**Growth inhibition**(comparison of area under growth curve)	EC_{50} (0-72 h) > 100 mg/L NOEC (0-72 h) > 100 mg/L
(2)**Growth inhibition**(comparison of growth rates)	EC_{50} (24-48) > 100 mg/L EC_{50} (24-72) > 100 mg/L NOEC (24-72) > 100 mg/L

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:** Experimental design and analytical procedure were well documented. Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed :**
- **Order number forsorting :**
- **Remarks field for GeneralRemarks :**

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g., *DAPHNIA*) (1)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nuoplaz 6965

METHOD

- **Method:** ASTM and USEPA
- **Test type:** Flow-through condition
- **GLP:** Yes
- **Year:** 1984
- **Analytical procedures:** Yes. Measured by GLC, on 0,4,7,14,21day)
- **Species/Strain:** *Daphnia magna*
- **Test details:** Dynamic flow-through
- **Statistical methods:** ANOVA, 2WANOVA, arcsin transformation and Fisher's protected Least Significant Difference (LSD)

Remarks field for Test Conditions:

Test organisms: Source; in house culture
Age at study initiation: Juveniles within 24h old.
Control group: Yes (control and solvent control)

Test conditions: Dilution Solvent for Concentrated stock standards : Acetone (1.049mg/mL)
A proportional diluter system was used for the intermittent introduction of test material and dilution water into the test chambers.
Test temperature range: 18-22 °C (average temperature 20°C).
Well water was delivered to the chambers as a minimum rate of 2.0mL/min.
Exposure vessel type: 900mL test solution in a 1000 mL glass beaker; 4 beakers per treatment
Dilution water chemistry: Hardness and other characteristics are reported.
Dilution water pH in test: pH=8.3-8.4.
Lighting: 37-74 footcandles, 16h:8h light-darkness cycle
Feeding: Algae (Selenastrum capricornutum) three times a day
Supplemented with a trout chow suspension at least twice a week

Element (unit) basis: Mean cumulative numbers of juveniles produced per adult (reproduction)
Growth (length) of parental Daphnia
Long-term survival

Test design: Number of replicates=4; individuals per replicate=10;
Method of calculating mean measured concentrations Geometric mean.

Exposure period: 21 d

Analytical monitoring: By GLC analysis. 33-101% of the nominal concentration at Preparation

RESULTS

- **Nominal concentrations:** 0, 0.0074, 0.012, 0.027, 0.048, 0.100 mg/L
- **Measured concentrations:**

Measured concentration of test chemical during 21-day exposure

Nominal concentration (mg/L)	Measured concentration (day, mg/L)					
	0	4	7	14	21	mean

Control	ND	ND	ND	ND	ND	ND
Solvent Cont.	ND	ND	ND	ND	ND	ND
0.0074	0.00328	0.00366	0.00558	0.00246	0.00482	0.0040
0.012	0.00748	0.00626	0.00843	0.00478	0.00747	0.0069
0.027	0.0172	0.0150	0.0204	0.0110	0.0157	0.0159
0.048	0.0305	0.0252	0.0371	0.0176	0.0348	0.029
0.100	0.0824	0.0766	0.0870	0.0630	0.1011	0.082

Cumulative Number of Dead Parental *Daphnia.*

Nominal conc.	Days									
(mg/L)	0	3	5	7	10	12	14	17	19	21
Control	0	0	0	0	0	0	0	1	1	2
Solvent Cont.	0	0	0	0	0	1	1	2	3	4
0.0074	0	0	0	0	0	1	1	1	1	1
0.012	0	0	0	0	0	0	0	0	0	0
0.027	0	0	0	0	0	0	0	0	0	0
0.048	0	0	0	0	1	1	1	1	1	1
0.100	0	0	0	0	0	0	0	0	0	0

Mean Growth data of Parental *Daphnia* (21-d)

Nominal conc. (mg/L)	Replicate A	Replicate B	Replicate C	Replicate D
Control	58.6 (n=9)	58.4 (n=9)	58.8 (n=10)	58.5 (n=10)
Solvent Cont.	59.1 (n=7)	59.0 (n=10)	59.0 (n=9)	59.3 (n=10)
0.0074	59.5 (n=10)	58.5 (n=10)	60.1 (n=9)	59.5 (n=10)
0.012	59.1 (n=10)	59.4(n=10)	59.5 (n=10)	59.8 (n=10)
0.027	59.8 (n=10)	58.4 (n=10)	59.9 (n=10)	60.3 (n=10)
0.048	59.6 (n=10)	59.6 (n-10)	59.7 (n=9)	58.6 (n=10)
0.100	58.7 (n=10)	60.0 (n=10)	58.8 (n=10)	59.0 (n=10)

Mean numbers of instar produced during 21-d.

Nominal conc.	Days									
(mg/L)	0	3	5	7	10	12	14	17	19	21
Control	-	-	-	-	109	196	317	86	179	170
Solvent Cont.	-	-	-	16	164	178		240	75	156
0.0074	-		-	3	141	202	302	261	75	274
0.012	-		-	3.5	122	206	373	221	96	265
0.027	-	-	-	8.3	150	189	317	218	138	313
0.048	-	-	-	-	113	203	242	120	233	214
0.100	-	-	-	5.3	135	186	223	180	93	269

Statistical results as appropriate:

Calculated LC_{50} Value for Parental *Daphnia:* LC_{50}(21day) >0.082(mg/L)

Calculated EC_{50} value for Inhibition of Reproduction: EC_{50}(21day) > 0.082(mg/L)

Remarks field for Results:

Biological observations

Cumulative numbers of dead parental *Daphnia*: Control: 2 (mortality: 5%).
Solv. Cont.: 4 (mortality: 10%)
0.0074 mg/L: 1 (mortality: 2.5%)
0.012 mg/L: 0 (mortality: 0%)
0.027 mg/L : 0 (mortality: 0%)
0.048 mg/L: 1 (mortality: 2.5%)

0.100 mg/ L : 0 (mortality: 0%)

Time of the first production of juveniles: Control : 7-10d
Solvent control: 5-7d
0.0074 mg/L : 5-7d
0.012 mg/L: 5-7d
0.027 mg/L : 5-7d
0.048 mg/L: 7-10d
0.100 mg/ L : 5-7d

Mean cumulative numbers of juveniles produced per adult alive for 21days:
Control : 112.7
Solvent control: 168.5
0.0074mg/L : 119.6
0.012 mg/L: 139.3
0.027 mg/L : 133.3
0.048 mg/L: 116.0
0.100 mg/L 112.9

Was control response satisfactory: Yes.

CONCLUSIONS

·NOEC (21-d, reproduction) : 0.082 mg/L,
·LOEC (21-d, reproduction) : >0.082 mg/L,
·EC_{50} (21-d, reproduction) : >0.082 mg/L;
·LC_{50} for parental *Daphnia* (21-d) : >0.082 mg/L

DATA QUALITY

- **Reliabilities:**
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Analytical Biochemistry Laboratories, Inc.,

REFERENCES

CMA Doc. I.D. 40-8565036 (1985).

OTHER

- **Last changed :**
- **Order number forsorting :**
- Remarks field for GeneralRemarks :

CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g., *DAPHNIA*) (2)

TEST SUBSTANCE

• **Identity:**	Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
• **Remarks:**	Source: Tokyo Kasei Kogyo Co., Ltd. Lot No. AX01 Purity: >95.0%

METHOD

• **Method:**	OECD TG 211 (revised edition of No.202).
• **Test type:**	Semi-static.
• **GLP:**	Yes
• **Year:**	1998
• **Analytical procedures:**	Yes. Measured by HPLC 2-3 times a week (before and after the replacement of the test water)
• **Species/Strain:**	*Daphnia magna*
• **Test details:**	Semi-static (water renewal: 3 times a week), open-system.
• **Statistical methods:**	Eco-Statics (Version 1.0 beta-edition R1.4)

Remarks field for Test Conditions:

Test organisms:	Source, supplier, any pre-treatment, breeding method: Supplied by NIES (Japan). Age at study initiation: Juveniles within 24h old. Control group: Yes.
Test conditions	Stock solutions preparation and stability: No solvent used. Test chemical was diluted to 1.0wt.% (with solubilizer HCO-40 1.0wt.% controlled) with diluting water (Elendt M4) before use. Solubilizer concentration was controlled 100mg/L with working solution (HCO-40 1.0wt.%). Test temperature range: 19. 9-20.8 °C (average temperature 20°C). Exposure vessel type: 80mL test solution in a 100 mL glass beaker; 10 beakers per treatment Dilution water source: Elendt M4(OECD guideline No.211 Annex 2) Dilution water chemistry: Hardness: 251mg/L as $CaCO_3$ Lighting: <1 ,200 lx, 16h:8h light-darkness cycle Water chemistry in test: DO= 7. 0-9.2mg/L; pH=7.4-7.9. Feeding: *Chlorella regularis*, 0.1-0.2 mgC/day/individual
Element (unit) basis:	Mean cumulative numbers of juveniles produced per adult (reproduction)
Test design:	Number of replicates=10; individuals per replicate=10; Concentrations: 0, 55.6, and 100 mg/L, because 48h-EiC_{50} for parent Daphnia (Acute immobilization test) was>180mg/L. Dispersant control was also tested.
Method of calculating mean measured concentrations:	Geometric mean.
Exposure period:	21 d
Analytical monitoring:	By HPLC analysis. 99.7-101.3% of the nominal concentration at preparation; 94.7-99.3% just before the renewal of the test water (after 2 days exposure).

RESULTS

- **Nominal concentrations:** 0, 55.6, 100 mg/L
- **Measured concentrations:** Time-weighted measured concentrations of test chemical during a 21-day exposure were 54.8 and 98.7 mg/L.

Measured concentration of test chemical during 21-day exposure

Nominal concentration	Measured concentration (day, mg/L)					
(mg/L)	0(new)	2 (old)	7(new)	9(old)	16(new)	19(old)
Control	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0	< 1.0
Disp.Cont.	< 1.0	<1.0	< 1.0	< 1.0	< 1.0	< 1.0
55.6	56.3	54.4	55.4	53.9	56.3	52.6
100	100.4	99.3	100.0	98.5	99.8	95.2

new: freshly prepared test solutions.
old: test solution after 2 days exposure.

- **Unit :** mg/L
  - NOEC (21-d, reproduction) : 55.6 mg/L,
  - LOEC (21-d, reproduction) : >100 mg/L,
  - EC_{50} (21-d, reproduction) : 89.1 mg/L;
  - LC_{50} for parental *Daphnia* (21-d) : >100 mg/L; calculated based on nominal concentrations.

Cumulative Number of Dead Parental *Daphnia*.

Nominal conc.	Days																				
(mg/L)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Disp.Cont.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
55.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	2	2

Mean cumulative numbers of juveniles produced per adult during 21-d.

Nominal conc.	Days																				
(mg/L)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.8	2.2	7.1	7.7	8.2	19.6	20.4	23.2	43.8	48.0	61.6	83.0	88.0	88.7
Disp.Cont.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.3	8.2	8.2	8.7	29.2	31.9	33.0	55.8	61.5	64.8	72.0	73.8	73.8
55.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.0	2.0	2.7	5.1	9.3	13.6	26.6	34.4	43.9	51.4	66.2	74.3	79.9
100	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6	2.6	3.6	7.8	9.3	11.0	15.1	17.5	20.3	30.3	33.0	33.0

Cumulative Number of Juveniles produced per Adult Alive for 21-d.

	Nominal Concentration(mg/L)			
Vessel No.	Cont.	Disp.Cont.	55.6	100.0
1	74	74	68	37
2	57	71	70	25
3	126	92	65	-
4	127	78	96	-
5	90	73	89	36
6	84	70	116	29
7	71	76	78	35
8	94	84	93	28
9	78	75	87	34
10	86	45	37	40
Mean (S.D)	88.7(22.524)	73.8(12.072)	79.9(21.533)	33.0(5.127)
Inhibition rate(%)		0.832	0.901	0.372

Significant difference*1 **

-:were not calculated because the parental *Daphnia* was dead during a 21-days testing period.
1*:Indicates a significant difference by Dunnet multiple comparison procedure, Two-sides test.
**:Indicates a significant difference (alpha=0.01) from the control.

- **Statistical results as appropriate:**
  Calculated LC_{50} Value for Parental *Daphnia:* LC_{50}(21day) >100(mg/L)
  Calculated EC_{50} value for Inhibition of Reproduction: EC_{50}(21day) = 89.1(mg/L)
  (Statistical method: Logit)

Remarks field for Results :

Biological observations

Cumulative numbers of dead parental *Daphnia*: Control: 0 (mortality: 0%),
Disp.Cont.: 0(mortality: 0%)
55.6 mg/L: 0(mortality: 0%)
100 mg/L: 2 (mortality: 20%)

Time of the first production of juveniles: 8-13d for control
8-12d for dispersant control
8-13d for 55.6 mg/L
10-14d for 100 mg/L

Mean cumulative numbers of juveniles produced per adult alive for 21days:
Control: 88.7, Dispersant control: 73.8
55.6 mg/L: 79.9, 100 mg/L: 33.0

Was control response satisfactory: Yes. Mean cumulative numbers of juveniles produced per adult was 88.7 and 73.8 > 60.

CONCLUSIONS

- NOEC (21-d, reproduction) : 55.6 mg/L,
- LOEC (21-d, reproduction) : >100 mg/L,
- EC_{50} (21-d, reproduction) : 89.1 mg/L,
- LC_{50} for parental *Daphnia* (21-d) : >100 mg/L; calculated based on nominal concentrations.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Experimental design and analytical procedure were well documented.
  Carried out by Toray Research Center (Japan).

REFERENCES

Environment Agency of Japan (1998).

OTHER

- **Last changed :**
- **Order number for sorting :**

- **Remarks field for GeneralRemarks:**

HEALTH ELEMENTS

ACUTE ORAL TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0%
  Kept at room temperature in a dark place until use. Stability of mixture of dose was confirmed for 7 days under 4C.

METHOD

- **Method:** OECD TG 401
- **Test type:** Single Dose Oral Toxicity Test
- **GLP:** Yes
- **Year:** 1996
- **Species:** Rat
- **Strain:** Crj: CD(SD)
- **Route of administration:** Oral (by single-dose gavage)
- **Doses/concentration levels:** 0(vehicle) and 2,000 mg/kg
- **Sex:** Male & Female
- **Vehicle:** Corn oil
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
Age at study initiation: 6 weeks old for both sexes.
Weight at study initiation: 149-163 g for male.
126-140 g for female
No. of animals per sex per dose: 5 per sex per dose group

Study Design:
Vehicle: Corn oil. 40.0w/v% for 2000 mg/kg.
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
Each rat was weighed immediately prior to treatment,7 and 14 days after post-treatment observation period. The rats were observedeach hour to 6hr, after that, 2 times for one day during this time for signs of toxicity.

RESULTS

- **LD_{50}:** Male : > 2,000 mg/kg
  Female : > 2,000 mg/kg

REMARKS FIELD FOR RESULTS.

Body weight: The test substance did not cause any changes in body weight.
No detailed body weight data available.
Food/water consumption: No detailed data available.
Clinical signs : Loosening erring of the stool attributable to the treatment with corn oil was observed for 3 hours from the administration for both sexes in the groups given 0 and 2000 mg/kg. However, no deaths occurred of either male or female animals.
Haematology: Not done
Biochem: Not done.
Ophthalmologic findings: Not examined.
Mortality and time to death: No deaths were recorded in treated and control group.
Gross pathology incidence and severity: No macroscopic abnormalities that could be attributes to treatment with the test substance were seen on pathological examination.
Organ weight changes: Not done.
Histopathology (incidence and severity): Not done.

CONCLUSIONS

LD_{50} was established at > 2,000 mg/kg for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by the Biosafety Research Center, Food, Drugs and Pesticides (An-pyo Center), Japan

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.4(1996)

Ministry of Health & Welfare, Japan

GENERAL REMARKS

ACUTE INHALATION TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz 6959, Batch No. 39049
  Purity: 98.95%

METHOD

- **Method:** Not specified
- **GLP:** Yes
- **Year:** 1982
- **Species:** Rat
- **Strain:** Crj: CD(SD)
- **Doses/concentration levels:** 2,600 mg/m^3
- **Sex:** Male & Female
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:

Age at study initiation: Not stated.
Weight at study initiation: 210-275 g for both sexes.
No. of animals per sex per dose: 5 per sex per dose group

Study Design:

Inhalation Chamber: A 0.5m^3 stainless steel inhalation chamber was used. (Youg and Bertke, Cincinnati, Ohio)
The test compound atmosphere was generated directly into the chamber by means of Jet Nebulizer Mechanism. Chamberconcentrations were monitored by a filter paper/gravimetric techniqueapproximately every 30 min during the exposure period.
The HEPA filtered chamber air-flow was maintained between 10 to 20 air changes per hour during the exposure period with the chamber under slightly negative pressure.
The temperature in the chamber was maintained at 69-75 degree F with relative humidity of 30-50%
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
After the exposure, all animals were observed daily for 14 days for clinical signs of toxicity. Body weights were recorded prior to exposure and weekly thereafter. All animals were subjected to necropsy at termination of the study.

RESULTS

- LD_0: Male : > 2,600 mg/m^3

Female : > 2,600 mg/m^3

REMARKS FIELD FOR RESULTS.

Body weight: The test substance did not cause any changes in body weight.

Mean body weight(g) of rats exposed to this chemical			
Males	Initial weight	265.1(8.40)	
	First week	297.8(14.02)	
	Second week	329.7(15.27)	
Females	Initial weight	213.9(2.66)	
	First week	223.2(3.96)	
	Second week	238.1(4.82)	Mean(S.D.)

Food/water consumption: No detailed data available.
Clinical signs : All animals (male and female) had matted, drenched coats for the first 2 days, otherwise no visible signs.
Haematology: Not done
Biochem: Not done.
Ophthalmologic findings: Not examined.
Mortality and time to death: No deaths were recorded.
Organ weight changes: Not done.
General necropsy observations: All males and 3/5 females exhibited reddening patches on lungs.

CONCLUSIONS

LD_0 was 2,600 mg/m^3 for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by Midwest Research Institute.

REFERENCES

Nuodex Inc. Acute inhalation toxicity test in SpragueDawley rats using compoundNouplaz 6959

Environmental Protection Agency (1983)

GENERAL REMARKS

ACUTE DERMAL TOXICITY

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz 6959, Batch No. 39049
  Purity: 98.95%

METHOD

- **Method:** Procedure set forth in the Federal Insecticide, Fungicide, andRodenticide Act (FIFRA)
- **GLP:** Yes
- **Year:** 1981
- **Species:** Rabbits
- **Strain:** New Zealand albino white rabbits
- **Doses/concentration levels:** 2.0 mL/kg
- **Sex:** Male & Female
- **Post exposure observation period:** Two weeks.
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:

Age at study initiation: Not stated.
Weight at study initiation: 2.3-3.2 kg for both sexes.
No. of animals per sex per dose: 3 per sex per dose group and 2 per sex for control.

Study Design:

Procedure: 24 hours prior to treatment the hair on the back of each rabbit was clipped so as to expose approximately 10% of the body surface area. Before dosing, epidermal abrasions were made longitudinally over the exposure area. The abrasions were sufficiently deep to penetrate the stratum corneum but not so deep as to cause bleeding.
A dosage was applied to the exposure area. A 2 x 2-inch gauze pad was placed on the exposure area to prevent seepage of the compound from the area. Each animal was then wrapped with a rubber dam. After 24 hour of exposure, the rubber dam and gauze pad were removed, and the exposure area was wiped to remove any remaining test material.
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
After the exposure, all animals were observed daily for 14 days for clinical signs of toxicity. A gross necropsy was performed on all animals at the end of the 14 day observation period.

RESULTS

- **LD_{50}:** Male : > 2.0 mL/kg
  Female : > 2.0 mL/kg

REMARKS FIELD FOR RESULTS.

Body weight: The test substance did not cause any changes in body weight.

Individual Animal Boy Weights

	Sex	Body weight (kg)		
Control		day 1	day 7	day 14
	male	3.2	3.4	3.6
		3.2	3.4	3.6
	female	2.7	3.0	3.1
		2.9	3.1	3.3
2.0 mL/kg	male	2.3	2.3	2.5
		2.4	2.4	2.5
		2.3	2.2	2.4
	female	2.3	2.5	2.7
		2.4	2.6	2.7
		2.4	2.5	2.6

Food/water consumption: No detailed data available.
Clinical signs : No toxic sign.
Haematology: Not done
Biochem: Not done.
Ophthalmologic findings: Not examined.
Mortality and time to death: No deaths were recorded.
Organ weight changes: Not done.
Gross Pathology: Nothing noted.

CONCLUSIONS

LD_{50} was 2.0 mL/kg for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out by Midwest Research Institute.

REFERENCES

Nuodex Inc. Acute dermal toxicity test of Tenneco Chemicals Inc. compound Nouplaz 6959 in rabbit.

Environmental Protection Agency (1981)

GENERAL REMARKS

SKIN IRRITATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz TOTM(Tenneco Chemicals, Inc.)
  Purity: 98.95%

METHOD

- **Method:** The test method was similar to Section 1500.41.Federal Hazardous Substances Act Regulations - 16 CFR
- **GLP:** Yes
- **Year:** 1981
- **Species:** Rabbits
- **Strain:** New Zealand albino white rabbits
- **Doses/concentration levels:** 0.5 mL
- **Sex:**
- **Post exposure observation period:** 24, 72 hours
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Husbandry Conditions Temperature - 70 ± 2 degree F
Relative Humidity - 45% ± 5%
Light - 12 hour light/dark cycle
Diet - Wayne 15% Rabbit Ration and tap water are provided ad libitum. Based on our current knowledge no contaminants are known to be in this diet or water that might be expected to interfere with the objectives of the study.
Caging - Stainless steel with elevated wire mesh flooring 1 rabbit/cage
Bedding - Techbord
Shepherd Products Company
Kalamazoo, Michigan 49005

Test method: A 0.5 mL portion of material was applied to an abraded and an intact akin site on the same rabbit. Gauze patches were then placed over the treated areas and an impervious material was wrapped snugly around the trunks of the animals to hold the patches in place.
The wrapping was removed at the end of the twenty-four (seventy two) hour period and the treated area were examined. TheDraize method of scoring was employed.

Evaluation: Draize Scale For Scoring Reactions

Erythema and Eschar Formation:	Value
No erythema	0
Very slight erythema(barely perceptible)	1
Well defined erythem	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slighteschar formation (injuries in depth)	4

Edema Formation	Value
No edema	0
Very slight edema(barely perceptible)	1
Slight edema(edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1millimeter)	3
Severe edema (raised more than 1 millimater and extending beyond the area of exposure)	4

RESULTS

- **Primary Irritation Score : 4.16/4 =1.04**

REMARKS FIELD FOR RESULTS.

Erythema and Eschar Formation	Reading (Hours)	Rabbit Number 1	2	3	4	5	6	Average
Intact skin	24	2	1	2	1	2	1	1.50
Intact skin	72	0	0	1	0	0	0	0.17
Abraded skin	24	2	1	2	1	2	1	1.50
Abraded skin	72	0	0	1	1	0	0	0.33
						Subtotal		3.50
Edema Formation								
Intact skin	24	1	0	0	0	1	0	0.33
Intact skin	72	0	0	0	0	0	0	0.00
Abraded skin	24	1	0	0	0	1	0	0.33
Abraded skin	72	0	0	0	0	0	0	0.00
						Subtotal		0.66
						Total		4.16

CONCLUSIONS

Slightly irritating
This report concluded that TOTM was not a primary skin irritant in rabbit.
It is not possible to assign a classification.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1= reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study, carried out byBiosearch Inc.

REFERENCES

Nuodex Inc. Primary Skin Irritation - Rabbits. OTS 20657758. Doc ID 878214470,1981

GENERAL REMARKS

EYE IRRITATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz TOTM(Tenneco Chemicals, Inc.)
  Purity: 98.95%

METHOD

- **Method:** The test method was similar to Section 1500.42.Federal Hazardous Substances Act Regulations - 16 CFR.
- **GLP:** Yes
- **Year:** 1981
- **Species:** Rabbits
- **Strain:** New Zealand albino white rabbits
- **Numbers of animals** 6
- **Doses/concentration levels:** 0.1 mL
- **Sex:**
- **Post exposure observation period:** 1,2,3,4,7 days
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Husbandry Conditions Temperature - 70 ± 2 degree F
Relative Humidity - 45%± 5%
Light - 12 hour light/dark cycle
Diet - Wayne 15% Rabbit Ration and tap water are provided ad libitum. Based on our current knowledge no contaminants are known to be in this diet or water that might be expected to interfere with the objectives of the study.
Caging - Stainless steel with elevated wire mesh flooring 1 rabbit/cage
Bedding - Techbord
Shepherd Products Company
Kalamazoo, Michigan 49005

Test method: 0.1 mL of the experimental material was instilled into the right eyes of the test animals while the other eyes remained untreated to severe as controls. The treated eyes were examined at one, two, three, four and seven days Following instillation of the test materials into the eyes.

Evaluation: Interpretation of the results was made in accordance with theDraize Scale of Scoring Ocular Lesions.

Scale of Scoring Ocular Lesions

	Value range
(1) CORNEA	
A. Opacity - Degree of Density(area most dense taken for reading)	0 - 4
B. Area of Cornea Involved	1 - 4
Score equals A x B x 5 (Total Maximum = 80)	
(2) IRIS	

A. Values 0 - 2

Score equals A x 5 (Total Maximum = 10)

(3) CONJUNCTIVAE

A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris) 0 - 3

B. Chemosis 0 - 4

C. Discharge 0 - 3

Score equals (A+B+C) x 2 (Total Maximum =20)

RESULTS

- **Average Ocular IrritationScore : 2.3(1 day), 1.7(2day), 0(3,4,7day)**

REMARKS FIELD FOR RESULTS.

Rabbit number	Tissue	Reading 1 day	2 day	3 day	4 day	7day
1	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
2	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	4	2	0	0	0
	Total Ocular Irritation Score	4	2	0	0	0
3	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
4	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
5	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	2	0	0	0
	Total Ocular Irritation Score	2	2	0	0	0
6	(1) Cornea total	0	0	0	0	0
	(2) Iris total	0	0	0	0	0
	(3) Conjunctivae total	2	0	0	0	0
	Total Ocular Irritation Score	2	0	0	0	0
	Average Ocular Irritation Score	2.3	1.7	0.0	0.0	0.0

CONCLUSIONS

Slightly irritating

This report concluded that TOTM was not a primary skin irritant in rabbit.

It is not possible to assign a classification.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

Well conducted study, carried out by Biosearch Inc

REFERENCES

Nuodex Inc. Primary Eye Irritation - Rabbits. OTS 2065758. Doc ID 878214471,1983

GENERAL REMARKS

SENSITIZATION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nouplaz TOTM(Tenneco Chemicals, Inc.)
  Purity: 98.95%

METHOD

- **Method:** Buehler teat
- **GLP:** Yes
- **Year:** 1981
- **Species:** Guinea pig
- **Strain:** Albino guinea pig
- **Numbers of animals** 10
- **Doses/concentration levels:** 0.5 mL
- **Sex:** male
- **Post exposure observation period:** 10 application
- **Statistical methods:** Not applicable because of no fatality.

REMARKS FIELD FOR TEST CONDITIONS

Husbandry Conditions Temperature – 70 ± 2 degree F
Relative Humidity– 45% ± 5%
Light – 12 hour light/dark cycle
Diet – Charless River Guinea Pig Furmula and tap water are provided ad Libitum. Based on our current knowledge no contaminants were Known to be in this diet or water that might be expected to Interfere with the objectives of the study.
Caging – Stainless steel with elevated wire mesh flooring 5 guinea pigs/cage
Bedding – Deotized Animal CageBoard(DACB)
Shepherd Products Company
Kalamazoo, Michigan 49005

Test method: A 0.5 mL portion of material was applied to the intact akin test site on the guinea pigs. A gauze patch was placed over the treated area and an impervious material was wrapped snugly around the trunks of the animals to hold the patches in place. After a 24 hour contact period the patch was removed and the animals were allowed to rest for one day. Following this rest period another application was applied to the same skin site using a fresh sample. After the tenth application the animals were rested for a two week period. At the termination of the rest period a challenge application was put on skin sites differing from the original test sites. The challenge application remained on for 24 hours.
The sites were examined for reaction using the Draize method of scoring to grade reactions.

Evaluation: Draize Scale For Scoring Reactions

Erythema and Eschar Formation:	Value
No erythema	0

Very slight erythema(barely perceptible)	1
Well defined erythem	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slighteschar formation(injuries in depth)	4

Edema Formation:	Value
No edema	0
Very slight edema(barely perceptible)	1
Slight edema(edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1millimeter)	3
Severe edema (raised more than 1millimater and extending beyond the area of exposure)	4

RESULTS

- **No sensitization**

REMARKS FIELD FOR RESULTS.

		Reading After Application number										Challenge	
Guinea pig No.		1	2	3	4	5	6	7	8	9	10	24hours	48hours
1	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
2	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
3	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
4	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
5	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
6	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
7	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
8	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
9	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0
10	Erythema	0	0	0	0	0	0	0	0	0	0	0	0
	Edema	0	0	0	0	0	0	0	0	0	0	0	0

CONCLUSIONS

No senstization

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

  Well conducted study, carried out byBiosearch Inc.

REFERENCES

Nuodex Inc. Guinea Pig Contact Dermal Irritation/Sensitization-Modified Buehler Method *OTS 206574. Doc ID 878214475,1981*

GENERAL REMARKS

REPEATED DOSE TOXICITY (a)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Nuoplaz 6959
  Purity: 98.2% (GC/FID) 97.9% (HPLC)
  Impurities were detected at level than 0.1-0.5%, one being di(2-ethylhexyl) phthalate (DEHP).

METHOD

- **Method:** BIBRA Standard Operating Procedures
- **Test type:** Repeat Dose Toxicity
- **GLP:** Yes
- **Year:** 1984
- **Species:** Rat
- **Strain:** Fischer 344
- **Route of administration** Oral
- **Doses/concentration levels:** 0(0), 0.2(184), 0.67(650) and 2(1826) % (mg/kg bw/day)
- **Vehicle:** Rodent diet
- **Sex:** Male & Female
- **Exposure period:** 28 days
- **Frequency of treatment:** Once daily
- **Control group and treatment:** Dietary level 0% and reference compound DEHP 0.67%.
- **Post exposure observation period:** None
- **Duration of test:** Males and females; for 28 days
- **Statistical methods:** The control and TOTM treated groups were subject to analysis of variance, and if this was significant the treated groups were compared with the controls using the Least Significant Difference test.
  The controls and DEHP groups were compared using a two-tailed pooled student t test with Welch's correction. In all cased a probability level of $P<0.05$ was taken to indicate statistical significance.

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
Age at study initiation: 48-51 days old for males and females
Weight at study initiation: 137-154g for male.
111-132g for female.
No. of animals per sex per dose: 5 Rats per sex per dose group

Study Design:
Vehicle: Diet
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
Body wt. was recorded immediately prior to the first exposure and again for each animal 1, 3, 7, 10, 14, 17, 21, 24, 27 th days.
Twice each day the animals were observed in their cages forvariations in behaviour or condition, and once weekly a more detailed examination was made at the time of a weighing.

Food intakes were measured over the period day-3 to 0 and continuos intakes were measured at twice-weekly intervals until the day preceding autopsy. The intakes of test article or reference compound for each animal were calculated twice weekly using the analysed dietary concentrations of TOTM or DEHP, and the individual valued for bodyweight and food intake.

Hematologic parameters were evaluated for each animal.On the day preceding the start of the autopsies a sample of blood was collected from a caudal vein of each animal.

Autopsy: At the end of the 28th day treatment period the rats were deprived of food overnight, with water available. On the day of autopsy each animal was weighted and then killed. The blood was used to provide serum for clinical chemistry. During the autopsy any abnormalities of the external condition and of the thoracic or abdominal viscera were noted.

Organs: The weight of the following organs were recorded: adrenal glands, lungs, brain, ovaries, heart, spleen, kidneys, testes, liver, thyroid.

Electron microscopy: Two thin slices of liver, one from the left lobe, the other from the median lobe, were fixed for analysis. (The remainder of the liver was used for biochemical analysis.)

Biochemical analysis of the liver: Whole homogenateswere prepared and assayed for protein and cyanide-insensitivepalmitoyl-CoA.

RESULTS

- **NOAEL** 184 mg/kg bw
- **LOAEL** 650 mg/kg bw

REMARKS FIELD FOR RESULTS.

Body weight: No statistically significant differences of bodyweight between the control and TOTM or DEHP treated groups of either sex. There was a trend for the male rats from all the TOTM treated groups to be lighter than the controls. In the females, this trend was only evident in the 2.0% TOTM group.

Food/water consumption: Female rats fed 2.0% TOTM consumed significantly less diet than the controls during first seven days of treatment after which their intakes increased but remained lower than those of the controls. In the males there were no statistically significant differences between the control and TOTM fed groups during the treatment period.

Haematology : In both sexes haemoglobin concentration of the rats given diet containing 0.67 or 2.0% TOTM were statistically significantly lower than the control. In the males there was a small lowering of erythrocyte count in all groups given TOTM but this was not reproduced in the females.

Both sexes given the two higher dietary concentrations of TOTM had higher leucocyte counts than the control, but the differences were statistically significant only in the males. These male groups also had lower proportions of the leucocytes as eosinophils and monocytes.

Significantly lower values for haemotocrit and mean cell volume were limited to females given the two lower dose levels of TOTM.

Organ weights : In both sexes the liver weights, and liver weights relative to bodyweight, were

increased in the TOTM and DEHP treated animals compared to the controls. These differences were small and not statistically significant in the 0.2% TOTM group. The increase seen in the rats given2.0% TOTM was less than that in those given DEHP. In the males fed TOTM the higher values for brain weights relative to body weight, in the absence of any significant differences in the recorded weight probably reflect the lower bodyweights in the groups concerned. In the females there were statistically significant higher lung weights in the rats fed 0.2 or 0.67% TOTM when compered to the controls. In the case of the TOTM treatedanimals this difference was not dose related and not statistically significant when expressed relative to bodyweight.

Serum analyses : Analysis of serum from the males and females showed statistically significantly increased levels of albumin in the groups given 0.67 or 2.0% TOTM. In the males there were statistically significantly higher cholesterol levels in the 0.67 and 2.0% TOTM groups.

Concentrations of serum urea were statistically significantly increased in the male 2.0% TOTM group to the control values. In the females there was also an isolated statistically significantly lower value for lipid concentration in the 0.2% TOTM group.

Liver Biochemistry: Neither TOTM or DEHP treatment influenced to a statistically significant degree the concentration of hepatic protein. After TOTM treatmentPCoA activity was statistically significantly higher than controls in both sexes at the highest dose and in the males at the lower two doses. In the groups given TOTM only the highest dose level males had statistically significant increases of enzyme level. Both sexes given 0.67 or 2.0% TOTM had statistically significantly increased carnitine acetyltransferase activity with little difference between the two sexes.

Histology : No abnormalities were detected in themajority of the animals. The only lesions occurring with any frequency were focal interstitialpneumonitis and nephrocalcinosis in the females. The observations were not firmly dose related. Thepneumonitis was of limited extent, often only a single focus. Two female rats fed 2.0% TOTM showed reductions in sytoplasmic basophilia in liver although it was only marginal.

Electron Microscopy: In the hepatocytes from the control rats theperoxisomes varied in size from small to moderately large. They had uniformly electron dense contents and some possessed a lattice core. They were ubiquitously distributed throughout the cytoplasm. Feeding diet containing 2% TOTM produced a slight increase in the numbers of peroxisomes. which varied between cells. No difference was seen between the centrilobular and periportal areas.

CONCLUSIONS

The NOAEL for repeated dose toxicity is considered to be 184 mg/kg and the LOAEL is Considered 650 mg/kg for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

Well conducted study , carried out by the British Industrial Biological Research Associations

REFERENCES

Chemical Manufacturers Association, Project No. 3.0496. Report No. 0496/1/85

CMA Reference. TM-3.0-BT-B1B

GENERAL REMARKS

REPEATED DOSE TOXICITY (b)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use.

METHOD

- **Method:** Guidelines for 28-day Repeated Dose Toxicity Testing of Chemicals (Japan)
- **Test type:** Repeat Dose Toxicity
- **GLP:** Yes
- **Year:** 1996
- **Species:** Rat
- **Strain:** Crj:CD(SD)
- **Route of administration** Oral
- **Doses/concentration levels:** 0(vehicle), 100, 300 and 1,000 mg/kg/day
- **Vehicle:** Corn oil
- **Sex:** Male & Female
- **Exposure period:** 28 days
- **Frequency of treatment:** Once daily
- **Control group and treatment:** Vehicle (corn oil)
- **Post exposure observation period:** 2 weeks for 0 and 1,000 mg/kg/day dose.
- **Duration of test:** Males and females; for 28 days
- **Statistical methods:** Bartlett's test, Dunnett's test or Kruskal-Wallis test depending on whether or not the data were nonhomogeneous or homogeneous.
  Fisher 's test for the pathological result. Jonckheere's test for the correlation of dosage

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
Age at study initiation: 6 weeks old for males and females
Weight at study initiation: 130-151g for male.
110-121g for female.
No. of animals per sex per dose: 5 Rats per sex per dose group

Study Design:
Vehicle: Corn oil
Satellite groups and reasons they were added: None
Clinical observations performed and frequency:
Body wt. was recorded immediately prior to the first exposure and again for each animal every week
Hematologic parameters were evaluated for each animal. Bloodamples for the hematologic determinations were taken fromabdominal artery in rats after 16 hr fast. Clinical chemistry analyses were performed on serum samples from each animal. Urinalyses were performed for each rat. Urine samples were collected from each rat on the day prior to scheduled termination.
Organs examined at necropsy:

Organ weight: brain, liver, kidney, spleen,adrenal, spermary (male) and ovary (females) for each animal.
Microscopic: heart, liver, kidneys, spleen, adrenal and bone marrow from rats in the control and high-exposure groups and kidney from all dosage male.

RESULTS

- **NOAEL**

Male: >1,000 mg/kg/day
Female: >1,000 mg/kg/day

REMARKS FIELD FOR RESULTS.

Body weight: The mean body weight of treatment groups of rats for males and femalesnot Significantly different from controls at any time during the course of the study.
Food/water consumption: No significantly different from controls at any time during dosing and recoveringperiod for both sexes.
Clinical signs : No unusual clinical observations during the study.
Males: No dose-related change in general clinical signs.
Females: No dose-related change in general clinical signs.
Haematology :
at the end of dosing
Males and females: No dose-related significant changes inhematology.
In the blood clotting test, prothrombin times for males were slightly extended, but they were considered within the physiological change. For females, no significant changes in all test.
after recovering period
Males: In hematology, hemoglobin amounts for males at 1000mg/kg dosing were slightly increased, but they were considered within the physiological change. In the blood clotting test, no significant changes in all tests.
Females: No significant change in alltests.
Biochem :
at the end of dosing
Males: No dose-related significant adverse treatment-related effect in clinical chemistry.
Females: At 300, and 1,000 mg/kg dosing, chlorine contents were low.
after recovering period
Males: At 1,000 mg/kg dosing, potassium contents were slightly high.
Females: At 1,000 mg/kg dosing, GOT were slightly high.
But both changes were considered to be no meaning, because at the end of treatment these changes were not recognised
Urinalysis :
at the end of dosing
Males and Female: At 1,000 mg/kg dosing, some of rats (both sexes), amounts of urinary increased, but the mean urinary specific gravity values in the 1,000 mg/kg dosing group was not significant change from control group.
after recovering period:
Males and Females: No dose-related significant change in all tests.

Mortality and time to death: No deaths prior to scheduled termination.

Organ weight changes:

at the end of dosing

Male: No dose-related change in all testedorgans.

Female: Relative liver weight were slightly increased at 100 mg/kg dosing, but no dose-related change. Other organs, no significant change.

after recovering period:

Males: At 1,000 mg/kg dosing, relative kidneyweight were slightly low.

Female: At 1,000 mg/kg dosing, absolute and relative adrenal weight wereslightly high.

But both changes were consideredno related to dosing and recovering of this chemical.

Gross pathlogy and histopathlogy:

at the end of dosing:

Males: Coloured patch/zone of lungs were observed 1 of 100 mg/kg, 2 of 300 mg/kg and 3 animals of 1,000 mg/kg dosing group. Also hypertrophy of the kidney, hypertrophy of parathyroid, and etc. were observed. Amounts of eosinophilic body in the kidney were slightly increased in dosing group. But all these changes were considered no related the dosing and recovering of thischemical, because the degree and rate of changes were same of all the group included control.

Females: Red patch/zone of thymus dilated lumen of the uterus and etc. were observed. But all these changes were considered no related the dosing and recovering of this chemical, because the degree and rate of changes were same of all the group included control.

after recovering period:

Males and Females: No dose-related significant change in all tests.

CONCLUSIONS

No test substance related changes were noted in terms of clinical signs, body weight, food consumption, andhematology, blood chemicalexamination, urinalysis, and pathological findings.

The NOEL for repeated dose toxicity is considered to be 1,000 mg/kg/day for both sexes.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**

  Well conducted study , carried out by the Biosafety Research Center, Food, Drugs and Pesticides (An-pyo Center), Japan

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.4(1996)
Ministry of Health & Welfare, Japan

GENERAL REMARKS

TOXICITY TO REPRODUCTION

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-80301
  Purity: >99.0% Kept at room temperature in a dark place until use.

METHOD

- **Method:** OECD Preliminary reproductive toxicity screening test
- **Test type:** Preliminary reproduction toxicity screening test.
- **GLP:** Yes
- **Year:** 1998
- **Species:** Rat
- **Strain:** Crj;CD (SD)
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0(vehicle) 100, 300, 1,000 mg/kg/day
- **Vehicle:** Corn oil
- **Sex:** Male & Female
- **Administration period:** Male; for 46 days from 2 weeks prior to mating
  Female; from 2 weeks prior to mating to day 3of lactation
- **Frequency of treatment:** Once daily.
- **Control group and treatment:** Vehicle (corn oil)
- **Post exposure observation period:** None.
- **Terminal kill** Male: day 47
  Female: day 4 of lactation
- **Statistical methods:** Chi square test for 1 grade positive data and Fisher's test for another.
  Bartlett's test or Kruskal-Wallis' test for 2 or more grade positive data.
  And used Dunnett's test or Mann-Whitney's U-test for examination

REMARKS FIELD FOR TEST CONDITIONS

Test Subjects:
***Age at study initiation*:** 10 week old for both sexes.
***Weight at study initiation*:** 373-435 g for males, 217-257 g for females
***No. of animals per sex per dose*:** 12 per sex per dose group

Study Design:
The animals were sacrificed on the day 4 of lactation for females. Males and females with nomated were killed 1 day after the mating period. Females with no delivery killed 26th day of gestation period.
***Vehicle*:** Corn oil
***Satellite groups and reasons they were added*:** None
Mating procedures: Male/female per cage; 1/1, length of cohabitation;with in the limit of 14 days until proof of pregnancy (formation sperm detection in vagina) was observed.
***Clinical observations performed and frequency*:**
Parent: General appearance once a day

Foetus: General appearance once a day after birth

Organs examined at necropsy:

Parent: Males and females: Gross pathlogy of all organs were tested.

Males: Organ weight: Testis and epididymis of all animals.

Female: Organ weight: Ovary of all animals.

Count: Implantation sites and corpus luteum of ovary of all animals.

Microscopic: Males: Testis and epididymis. Count of sertoli sells, spermatocytes, round spermatids and elongate spermatids in seminiferous tubules of 5 animals of all dosing groups. (Stage I-VI, VII-VIII, IX-XI, XII-XIV of spermatozoon formative cycle.)

Females: Ovary

Pup : Gross pathlogy of all organs were tested. Dead pups and abnormal organs were tested histopathogy.

***Parameters assessed during study*:**

Body weight. Males: Prior to the first dosing and 2, 5, 7, 10, 14 day. After that once a week, the day sacrificed. Females: Prior to the first dosing and 2, 5, 7, 10, 14 day. During gestation period, 0, 1,3, 5, 7, 10, 17 and 20 day. During lactation period, 0, 1, and 4. During cohabitation period, the same day with male. Pups: Day 0 and 4

Food/water consumption. The same day when body wt. determined except lactation period and the day sacrificed for males, also, 0 day of gestation and lactation for female.

No. of pairs with successful copulation, copulation index (No.of pairs with Successful copulation/No. of pairs mated) x 100, duration of mating, No. of pregnant females, fertility index = (No.of pregnant animals/No. of pairs with successful copulation) x 100, No. of corpora lutea, No. of implantation sites, implantation index (No. of implantation sites/No. of corpora lutea) x 100, No. of pups born, delivery index (No.of pups born/No. of implantation sates)x 100, No. of love pups born, live birth index (No.of love pups born/No. of pups born) x 100, sex ratio of pups, No. of dead pups born, gestation length, gestation index (No. of females with live pops delivered/ No.of pregnant females) x 100, nursing index (No.of females nursing live pups/No.of females with normal delivery) x 100, No. of live pups on day 4, viability index (No.of live pups on day 4/No. of live pups born) x 100,

RESULTS

Repeat dose toxicity: NOEL 100 mg/kg/day for males
1,000 mg/kg/day for female

Reproductive and developmental toxicity: NOEL 100 mg/kg/day for males
1,000 mg/kg/day for female
1,000 mg/kg/day for offspring

REMARKS FIELD FOR RESULTS.

Mortality and day of death : None.
Body weight : No statistical significant difference from controls.
Food/water consumption: No statistical significant difference from controls.

Reproductive data : No statistical significant difference from controls.

Pups data : Body weight and weight gain of 300 mg/kg dosing group for both sexes were slightly low. But all pups of 100 and 1000 mg/kg dosing group were not statistical significant difference from controls.

At the other tests, no statistical significant difference from controls.

Grossly visible abnormalities, external, soft tissue and skeletal abnormalities :

For males:

Slightly decrease of spermatocytes and spermatids: 2 animals of 300 mg/kg dosing group.
11 of 1000 mg/kg dosing group.

Moderate decrease of spermatocytes and spermatids: 1 of 1000 mg/kg/dosing group.
At this animal, a few multinucleate giant cell were appeared and slightlyvacuolization of sertoli sells were observed. Also, at the epididymis, moderate amount of cell debris moderate decrease of spermatids and slightly granuloma of spermatic were observed.
For the control group, atrophy of seminiferous tubulewere observed 2 animals. At these animals, slightly amount of cell debris were observedone of these animals, slight decrease of spermatids was also observed.

Number of cells in seminiferous tubules:

Group 1(Stage I-VI) : Low value of spermatids at 300 mg/kg dosing group.
Low values of spermatocytes and spermatids at 1000 mg/kg dosing group.

Group 2(Stage VII-VIII):Low values of round spermatids and ratio of sertoli cells at 1000 mg/kg.

Group 3(stage IX-XI) :Low values of elongatespermatids and ratio of sertoli cells at 1000 mg/kg.

Group 4(stage XII-XIV) :Low values of spermatocytes, elongatespermatids, and ratio of sertoli cells at 1000 mg/kg dosing group.

For females:

Cyst of corpus luteum of ovary was observed 2 animals of 300 mg/kg dosing group.

No abnormal ovary observed at the female of 100 mg/kg dosing without successful copulation, females of control and 100 mg/kg dosing without pregnant.

Histopathological finding in rats

		dose (mg/kg)			
Items		**0**	**100**	**300**	**1,000**
No. of male animals examined		12	12	12	12
Organ: Findings					
	Grade				
Testis:					
Decrease, spermatocyte and spermatid	**Total**	0	0	2	12**
	+	0	0	2	11
	+ +	0	0	0	1
Multinuclear giant cell, seminiferous tubule	+	0	0	0	1
Vacuolozation, Sertoli cell	+	0	0	0	1
Atrophy, seminiferous tubule	+	2	0	0	0
Epididymis:					
Cell debris, lumen	**Total**	2	0	0	1
	+	2	0	0	0
	++	0	0	0	1
Decrease, sperm	**Total**	1	0	0	1
	+	1	0	0	0
	++	0	0	0	1
Granuloma, spermatic	+	0	0	0	1

No. of female animals examined		12	12	12	12
Ovary:					
Cyst, corpus luteum	<+>	0	0	2	0

Values are no, of animals with finding.
Grade: +=slight, ++=moderate change and <+>=detected
Significantly different from 0 mg/kg group: **:p ≦0.01.

Number of cells in seminiferous tubules of male rats.

Items	dose (mg/kg) 0	100	300	1,000
No. of animals examined	5	5	5	5
Group 1 (Stage I-VI)				
No. of Sertoli cells	20.12(3.18)	19.08(1.49)	18.52(1.45)	18.08(1.45)
Spermatogonia				
No.	16.80(5.65)	20.52(2.58)	18.48(3.17)	15.76(2.61)
ratio a)	0.85(0.29)	1.08(0.19)	1.01(0.21)	0.87(0.11)
Spermatocytes				
No.	50.80(7.44)	51.80(4.84)	42.64(2.63)	40.84(5.63)*
ratio	2.53(0.13)	2.72(0.26)	2.37(0.24)	2.25(0.16)
Round spermatids				
No.	138.36(17.20)	128.00(8.89)	117.68(5.59)*	112.60(3.11)**
ratio	6.91(0.35)	6.75(0.84)	6.39(0.70)	6.26(0.48)
Elongate spermatids				
No.	130.00(21.71)	132.32(11.17)	103.28(12.34)*	95.36(8.44)**
ratio	6.53(1.15)	6.98(0.88)	5.62(0.90)	5.30(0.69)
Group 2 (Stage VII-VIII)				
No. of Sertoli cells	16.96(2.63)	17.04(2.17)	16.64(2.73)	16.52(2.23)
Spermatogonia				
No.	2.92(1.06)	2.40(0.93)	2.04(0.68)	2.60(1.10)
ratio	0.18(0.09)	0.14(0.05)	0.12(0.03)	0.16(0.06)
Spermatocytes				
No.	91.68(10.37)	94.68(6.55)	84.44(6.99)	82.32(6.70)
ratio	5.45 (0.56)	5.60(0.51)	5.16(0.79)	5.03(0.54)
Round spermatids				
No.	142.08(13.39)	131.64(13.72)	123.96(8.23)	118.76(8.28)*
ratio	8.45(0.62)	7.75(0.39)	7.66(1.66)	7.25(0.62)*
Elongate spermatids				
No.	129.24(17.37)	128.32(16.88)	114.72(9.80)	105.65(13.47)
ratio	7.78(1.54)	7.56(0.72)	7.09(1.62)	6.46(1.05)
Group 3 (Stage VII-VIII)				
No. of Sertoli cells	19.28(1.92)	20.52(1.55)	19.20(1.58)	19.32(2.18)
Spermatogonia				
No.	4.52(1.32)	4.20(1.50)	4.92(1.63)	3.32(1.02)
ratio	0.23(0.05)	0.21(0.08)	0.26(0.11)	0.18(0.05)
Spermatocytes				
No.	102.52(10.83)	99.08(8.42)	97.56(4.50)	89.04(9.00)
ratio	5.34(0.56))	4.85(0.50)	5.10(0.36)	4.62(0.32)
Elongate spermatids				
No.	145.24(11.01)	130.64(9.90))	131.68(19.71)	119.24(15.90*
ratio	7.56(0.61)	6.37(0.23)	6.88(1.04)	6.21(0.83)*

Group 4 (Stage VII-VIII)				
No. of Sertoli cells	19.16(2.81)	20.92(1.73)	18.64(1.72)	16.72(0.92)
Spermatogonia				
No.	4.04(0.89)	3.72(0.72)	3.64(0.48)	3.64(0.71)
ratio	0.21(0.05)	0.18(0.03)	0.20(0.02)	0.22(0.05)
Spermatocytes				
No.	109.80(13.15)	110.36(9.22)	99.44(4.54)	88.76(4.33)**
ratio	5.76 (0.29)	5.28(0.12)	5.36(0.34)	5.32(0.46)
Elongate spermatids				
No.	159.76(15.91)	150.28(18.99)	137.08(17.70)	105.16(18.34)**
ratio	8.39(0.63)	7.19(0.71)	7.35(0.62)	6.33(1.31)**

Values are expressed as Mean(S.D.)

Significantly different from 0 mg/kg group; * $p \leqq 0.05$, ** $p \leqq 0.01$

a): (No. of spermatogenic cells/no. of sertoli cells in a seminiferous tubule)

Influence on reproductive performances of rats

	dose (mg/kg)			
Items	**0**	**100**	**300**	**1,000**
No. of male animals examined	12	12	12	12
No. of pairs with successful copulation	12	12	12	12
Duration of mating (day, Mean, (SD))	2.1(1.2)	2.3(1.3)	2.7(1.2)	2.7(1.1)
Copulation index(%)*	100.0	91.7	100.0	100.0
No. of pregnant animals	11	10	12	12
Fertility index(%)**	91.7	90.9	100.0	100.0

*(No.of pairs with successful copulation/no.of pairs mated) x 100

**(No. of pregnant animals/no.of pairs with successful copulation) x 100

Influence on developmental performances of rats

	dose (mg/kg)			
Items	**0**	**100**	**300**	**1,000**
No. of male animals examined	12	12	12	12
No. of corpora lutea	16.8(1.5)	17.3(1.3)	17.0(2.3)	17.9(2.2)
No. of implantation sites	15.5(1.7)	16.6(1.3)	16.0(2.0)	16.3(2.3)
Implantation index(%) [a]	92.5(7.2)	96.2(6.6)	94.5(8.4)	91.3(8.8)
No. of pups born(%)	13.7(3.1)	15.0(1.7)	15.0(1.8)	15.1(2.7)
Delivery index(%) [b]	87.6(15.4)	90.3(6.8)	94.1(7.2)	92.2(9.6)
Live pups born				
No.	13.3(2.9)	14.7(2.0)	14.9(2.0)	15.0(2.7)
Live birth index(%) [c]	97.1(5.6)	97.8(3.6)	99.2(2.6)	99.4(2.1)
Sex ratio(M/F)	1.09(0.69)	1.05(0.50)	1.17(0.75)	0.76(0.44)
Dead pups born				
No.	0.5(0.9)	0.3(0.5)	0.1(0.3)	0.1(0.3)
Gestation length(day)	22.7(0.5)	22.7(0.5)	22.5(0.5)	11.6(0.5)
Gestation index(%) [d]	100.0	100.0	100.0	100.0
Nursing index(%) [e]	100.0	100.0	100.0	100.0
Live pups on day 4				
No.	13.2(2.8)	14.6(2.1)	14.4(2.9)	14.5(2.9)
Viability index(%) [f]	99.5(1.8)	99.3(2.3)	95.6(11.5)	96.7(6.7)
Body weight of pups(g)				
Male Day 0	7.32(0.77)	7.13(0.52)	6.69(0.55)	6.87(0.84)
Day 4	11.71(1.76)	11.09(0.93)	10.23(0.98)*	10.60(1.47)
Day 0-4, gain(g)	4.39(1.04)	3.96(0.53)	3.54(0.77)*	3.73(0.80)
Body weight gain(%) [g]	59.41(8.87)	55.54(6.16)	53.19(11.91)	54.39(9.50)

Female	**Day 0**	6.93(0.83)	6.63(0.64)	6.33(0.58)	6.58(0.62)
	Day 4	11.08(1.71)	10.28(1.01)	9.84(1.01)*	10.03(1.46)
	Day 0-4, gain(g)	4.16(1.00)	3.65(0.56)	3.14(0.79)*	3.46(0.96)
	Body weight gain(%)	59.63(10.42)	55.24(8.07)	49.95(13.09)	52.17(11.10)

Values are expressed as Mean (S.D.)
Significantly difference from 0 mg/kg group ; $p \leqq 0.05$
a): (No. of implantation sites/no. of corpora lutea) x 100
b): (No. of pups born/no. of implantation sites) x 100
c): (No. of live pups born/no. of pups born) x 100
d): (No. of females with live pups delivered/ no. of pregnant females) x 100
e): (No. of females nursing live pups/no. of females with normal delivery) x 100
f): (No. of live pups on day 4/ no. of live pups born) x 100
g): (Body weight gain/body weight on day 0) x 100

CONCLUSIONS

Repeat dose toxicity

Histopathological examination of the testes, demonstrated decrease ofspermatocytes and spermatids in males of the 300 and 1000 mg/kg group. No effects of this chemical on general appearance, body weight, food consumption, autopsy findings, weights of the reproductive organs of both sexes, or histopathlogical features of the ovary were detected.

The NOELs are considered to be 100 mg/kg/day for males, and 1,000 mg/kg/day for females.

Reproductive and developmental toxicity

Except for the effects in males observed onhistopathological examination, no influence of this chemical was detected regarding reproductive ability, organ weight onhistopathological feature of the ovary, delivery or maternal behaviour of dams. No effects of this chemical were detected onviability, general appearance, body weights or autopsy findings for offspring.

The NOELs are considered to be 100 mg/kg/day for males, 1,000 mg/kg/day for females, and 1,000 mg/kg/day for offspring.

DATA QUALITY

- **Reliabilities:** Klimisch Code: 1=reliable without restrictions.
- **Remarks field for Data Reliability:**
  Well conducted study , carried out by the Safety Research Institute for Chemical Compounds Co., Ltd.(Japan)

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.6(1998)

Ministry of Health & Welfare, Japan

GENERAL REMARKS

GENETIC TOXICITY IN VITRO (BACTERIAL TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use.

METHOD

- **Method:** Guideline for ScreeningMutagenicity Testing of Chemicals(Japan) and OECD TG 471 and 472
- **Test type:** Reverse mutation assay
- **GLP:** Yes
- **Year:** 1996
- **Species/Strain:** *Salmonella typhimurium* TA100, TA1535, TA98, TA1537
  Escherichia coli WP2 *uvr*A
- **Positive controls:** -S9 mix, 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, WP2, TA98)
  Sodium azide (TA1535)
  9-Aminoacridine (TA 1537)
  +S9 mix, 20Aminoanthracene (five strains)
- **S9:** Rat liver, induced withphenobarbital and 5,6-benzoflavone
- **Statistical methods** No statistical analysis was done.

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

  ***Concentration*:** -S9: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (five strains)
  +S9: 0, 313, 625, 1,250, 2,500, 5,000 ug/plate (five strains)
  ***Number of replicates*:** 2
  ***Plates/test*:** 3
  ***Procedure*:** Plate incorporation method
  ***Solvent*:** Acetone
  ***Positive controls*:**
  -S9 mix, 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (TA100, WP2, TA98)
  Sodium azide (TA1535)
  9-Aminoacridine (TA 1537)
  +S9 mix, 20Aminoanthracene (five strains)

RESULTS

- **Cytotoxic concentration:**

  Toxicity was not observed up to 5,000 ug/plate in five strains with and without metabolic activation (S9 mix).

- Genotoxic effects:

	+	?	-
With metabolic activation:	[ ]	[ ]	[x]
Without metabolic activation:	[ ]	[ ]	[x]

REMARKS FIELD FOR RESULTS.

CONCLUSIONS

Bacterial gene mutation is negative with and without metabolic activation.

DATA QUALITY

- **Reliabilities:** Valid without restriction.

Remarks field for Data Reliability

Well conducted study, carried out byHatano Research Institute, Food and Drug Safety Center (Hadano, Japan).

REFERENCES

Toxicity Testing Reports of Environmental Chemicals,vol.4(1996)

Ministry of Health & Welfare, Japan

GENERAL REMARKS

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use

METHOD

- **Method:** Guideline for Screening Toxicity Testing ofChemicals (Japan)
- **Test type:** Chromosomal aberration test
- **GLP:** Yes
- **Year:** 1996
- **Species/Strain:** CHL/IU cell
- **Metabolic activation:** with and without S9 from rat liver, induced withphenobarbital and 5,6-benzoflavone.
- **Statistical methods** Fisher's exact analysis

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

For continuous treatment, cells were treated for 24 or 48 hrs without S9.
For short-term treatment, cells were treated for 6 hrs with and without S9 and cultivated with fresh media for 18 hrs.

Concentration: -S9 (continuous treatment): 0, 1.3, 2.5, 5.0 mg/mL
-S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
+S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
Plates/test: 2
Solvent: Acetone
Positive controls: Mitomycin C for continuous treatment
Cyclophosphamide for short-term treatment

RESULTS

- **Cytotoxic concentration:**

Toxicity was not observed up to 5.0 mg/ml in continuous and short-term treatment with or without S9 mix.

- **Genotoxic effects:**

	Clastogenicity			polyploidy		
	+	?	-	+	?	-
With metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]
Without metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]

REMARKS FIELD FOR RESULTS.

GENETIC TOXICITY IN VITRO (NON-BACTERIAL IN VITRO TEST)

TEST SUBSTANCE

- **Identity:** Tris(2-ethylhexyl)benzene-1,2,4-tricarboxylate
- **Remarks:** Source: Daihachi Kagaku Kogyo Co., Ltd. Lot. No. N-60601
  Purity: >99.0% Kept at room temperature in a dark place until use

METHOD

- **Method:** Guideline for Screening Toxicity Testing ofChemicals (Japan)
- **Test type:** Chromosomal aberration test
- **GLP:** Yes
- **Year:** 1996
- **Species/Strain:** CHL/IU cell
- **Metabolic activation:** with and without S9 from rat liver, induced withphenobarbital and 5,6-benzoflavone.
- **Statistical methods** Fisher's exact analysis

REMARKS FIELD FOR TEST CONDITIONS

- **Study Design:**

For continuous treatment, cells were treated for 24 or 48 hrs without S9.
For short-term treatment, cells were treated for 6 hrs with and without S9 and cultivated with fresh media for 18 hrs.

Concentration: -S9 (continuous treatment): 0, 1.3, 2.5, 5.0 mg/mL
-S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL
+S9 (short-term treatment): 0, 1.3, 2.5, 5.0 mg/mL

Plates/test: 2

Solvent: Acetone

Positive controls: Mitomycin C for continuous treatment
Cyclophosphamide for short-term treatment

RESULTS

- **Cytotoxic concentration:**

Toxicity was not observed up to 5.0 mg/ml in continuous and short-term treatment with or without S9 mix.

- **Genotoxic effects:**

	Clastogenicity			polyploidy		
	+	?	-	+	?	-
With metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]
Without metabolic activation:	[ ]	[ ]	[x]	[ ]	[ ]	[x]

REMARKS FIELD FOR RESULTS.

Appendix I
Parameters used in caluculation of distribution by Mackay level III fugacity model.

Physico-chemical Parameter for TOTM

molecular weight		546.79	Measured
melting point [°C]		-50	Measured
vapor pressure [Pa]		2.80E-04	Estimated
water solubility [g/m³]		0.13	Measured
log Kow		5.94	Measured
half life [h]	in air	12	Estimated
	in water	288	Estimated
	in soil	288	Estimated
	in sediment	864	Estimated

Temp. [°C] 25

Environmental Parameter

		Volume [m³]	depth [m]	area [m²]	organic carbon [—]	lipid content [—]	density [kg/m³]	residence time [h]
bulk air	air	1.0E+13					1.2	100
	particles	2.0E+03						
	total	1.0E+13	1000	1E+10				
bulk water	water	2.0E+10					1000	1000
	particles	1.0E+06			0.04		1500	
	Fish	2.0E+05				0.05	1000	
	Total	2.0E+10	10	2E+09				
bulk soil	Air	3.2E+08					1.2	
	Water	4.8E+08					1000	
	Solid	8.0E+08			0.04		2400	
	Total	1.6E+09	0.2	8E+09				
bulk sediment	Water	8.0E+07					1000	
	Solid	2.0E+07			0.06		2400	50000
	Total	1.0E+08	0.05	2E+09				

Intermadea Transport Parameter (m/h)

air side air-water MTC	5	soil air boundary layer MTC	5
water side air water MTC	0.05	sediment-water MTC	1E-04
rain rate	1E-04	sediment deposition	5E-07
aerosol deposition	6E-10	sediment resuspension	2E-07
soil air phase diffusion MTC	0.02	soil water runoff	5E-05
soil water phase diffusion MTC	1E-05	soil solid runoff	1E-08

Theoretical Distribution of TOTM

scenario 1

	emission rate [kg/h]	conc. [g/m³]	amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
Air	1,000	1.3.E-07	1.3.E+04	19.6	7.5E+02	1.3.E+02
Water	0	1.6.E-05	3.10.E+03	4.7	7.6E+00	3.1.E+00
Soil	0	2.5.E-03	4.4.E+04	66.2	1.1E+02	
Sediment		1.3.E-02	6.3.E+03	9.5	5.1E+00	1.2.E-01
		total amount	6.7.E+04			

scenario 2

	Emission rate [kg/h]	conc. [g/m³]	Amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
air	0	1.8.E-09	1.8.E+02	0.0	1.0.E+01	1.8.E+00
water	1000	9.7.E-04	1.9.E+05	32.7	4.7.E+02	1.9.E+02
soil	0	3.4.E-05	6.2.E+02	0.1	1.5.E+00	
sediment		7.9.E-01	3.9.E+05	67.2	3.2.E+02	7.9.E+00
		total amount	5.9.E+05			

scenario 3

	emission rate [kg/h]	conc. [g/m³]	Amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
air	0	7.0.E-13	7.0.E-02	0.0	4.1.E-03	7.0.E-04
water	0	5.2.E-08	1.0.E+01	0.0	2.5.E-02	1.0.E-02
soil	1000	2.3.E-02	4.2.E+05	100.0	1.0.E+03	
sediment		4.2.E-05	2.1.E+01	0.0	1.7.E-02	4.2.E-04
		total amount	4.2.E+05			

scenario 4

	emission rate [kg/h]	conc. [g/m³]	Amount [kg]	percent [%]	Transformation rate [kg/h]	
					Reaction	advection
air	600	7.8.E-08	7.8.E+03	3.0	4.5.E+02	7.8.E+01
water	300	3.0.E-04	6.0.E+04	23.5	1.5.E+02	6.0.E+01
soil	100	3.8.E-03	6.8.E+04	26.6	1.6.E+02	
sediment		2.4.E+01	1.2.E+05	46.9	9.8.E+01	2.4.E+00
		total amount	2.6.E+05			

I U C L I D

Data Set

Existing Chemical	:	ID: 67989-23-5
CAS No.	:	67989-23-5
EINECS Name	:	1,2,4-Benzenetricarboxylic acid, decyl octyl ester
EINECS No.	:	268-007-3
TSCA Name	:	1,2,4-Benzenetricarboxylic acid, decyl octyl ester
Molecular Formula	:	C10H22O.xC9H6O6.xC8H18O

Producer Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	02.11.2000

Substance Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	02.11.2000
Memo	:	ACC Phthalate Esters Panel HPV Testing Group
Printing date	:	13.12.2001
Revision date	:	
Date of last Update	:	30.10.2001
Number of Pages	:	11
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 OECD AND COMPANY INFORMATION

Type	:	lead organisation
Name	:	ACC Phthalate Esters Panel HPV Testing Group
Partner	:	Dr. Marian Stanley
Date	:	
Street	:	1300 Wilson Blvd.
Town	:	22209 Arlington, VA
Country	:	United States
Phone	:	(703) 741-5623
Telefax	:	(703) 741-6091
Telex	:	
Cedex	:	
Remark	:	The American Chemistry Council Phthalate Esters Panel sponsoring this test plan includes the following member companies: Eastman Chemical Company ExxonMobil Chemical Company Sunoco Chemicals Teknor Apex Company
Flag 26.10.2001	:	Critical study for SIDS endpoint

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	organic
Physical status	:	liquid
Purity 09.10.2001	:	% w/w

1.1.0 DETAILS ON TEMPLATE

Comment	This chemical is part of the Trimellitate category. The category includes the following four CAS numbers: 3319-31-1, 27251-75-8, 53894-23-8 and 67989-23-5.
Remark	DESCRIPTION OF THE TRIMELLITATES CATEGORY The trimellitates comprise a family of chemicals synthesized by esterifying trimellitic anhydride with alcohols with average carbon numbers ranging from approximately C7-C10, in the presence of an acid catalyst. The category includes the four trimellitates: 3319-31-1 (TOTM), 27251-75-8 (TIOTM), 53894-23-8 (TINTM), and 67989-23-5 (DOTM). Trimellitates in this category are all 1,2,4-benzenetricarboxylic acids with side chain ester groups ranging from C8 to C10. The structural formula for trimellitates varies somewhat depending on the isomeric composition of the alcohols used in their manufacture. The specific alcohols used are 2-ethylhexanol (TOTM), iso-octyl alcohol (TIOTM), iso-nonyl alcohol (TINTM), and a mixture of linear and branched decyl (40%) and octyl (60%) alcohols (DOTM). Trimellitates are colorless to slightly yellow liquids with high boiling points (> 250oC) and low vapor pressures; properties which contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils, but essentially insoluble in water. Because of the similarity in structure as well as physicochemical

properties, the trimellitates were grouped into a single category containing four substances with carboxylic side chain ester groups ranging from C8-C10.

Flag Critical study for SIDS endpoint
09.10.2001

1.7 USE PATTERN

Type : industrial
Category : Polymers industry
Remark : Trimellitates are used predominantly as plasticizers for production of flexible PVC. Because of their relatively high molecular weight (>500 g/mole) and bulky structure, they have lower volatility and greater resistance to migration than the corresponding phthalate ester plasticizers. They are predominantly used in the manufacture of high temperature PVC cables (Wilson, 1996). Since these chemicals are produced in closed systems, there is essentially no occupational exposure to these substances except at the flexible PVC production facility. Usually, these substances have been already blended to the compound as plasticizer, so it is not expected that downstream users or consumers are directly exposed to trimellitates.
Flag : Critical study for SIDS endpoint
13.12.2001 (3)

2.1 MELTING POINT

Value	:	234 °C
Decomposition	:	no at °C
Sublimation	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Melting point calculation by MPBPWIN ver. 1.40 using calculation methods of Joback and Gold and Ogle.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation Melting point calculation seems to give erroneously high results for the thhis class of chemicals.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(3) invalid

10.10.2001 (2)

2.2 BOILING POINT

Value	:	585 °C at 1013 hPa
Decomposition	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Boiling point calculation by MPBPWIN ver. 1.40 using calculation methods of Stein and Brown.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

10.10.2001 (2)

2.4 VAPOUR PRESSURE

Value	:	.0000000000014 hPa at 25° C
Decomposition	:	no
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Decomposition	:	no
Method	:	Vapor pressure calculation by MPBPWIN ver. 1.40 using calculation method of Grain.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

15.10.2001 (2)

2.5 PARTITION COEFFICIENT

Log pow	:	12.79 at 25° C
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Partition coefficient by LOGKOWWIN ver. 1.65 using an atom/fragment calculation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
20.12.2000		(2)

2.6.1 WATER SOLUBILITY

Value	:	2.78 other: ng/l at 25 ° C
Qualitative	:	
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Water solubility calculated using WSKOWWIN ver 1.36 based on Kow correlation method of Meylan and Howard
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
10.10.2001		(2)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spect.	:	nm
Rel. intensity	:	1 based on Intensity of Sunlight
Conc. of subst.	:	at 25 degree C
Indirect photolysis		
Sensitizer	:	OH
Conc. of sens.	:	1500000 molecule/cm3
Rate constant	:	.00000000000335 cm3/(molecule*sec)
Degradation	:	% after
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Photodegradation rate calculated by AOPWIN ver. 1.89 based on the methods of Atkinson.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

10.10.2001 (2)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	1 year at 25 degree C
t1/2 pH9	:	at degree C
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Hydrolysis rate calculated by HYDROWIN ver. 1.67 based on work for EPA by T. Mill et al.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

20.12.2000 (2)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	other
Air (level I)	:	0
Water (level I)	:	0
Soil (level I)	:	97.8
Biota (level II / III)	:	
Soil (level II / III)	:	
Method	:	other
Year	:	2000

Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
15.10.2001		(1)

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	other (calculation)
Year	:	2000
Result	:	Soil - 97.8% Air - 0.000000102% Water - 0.0000000179% Sediment - 2.17% Suspended sed. - 0.068%
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
20.12.2000		(1)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

6. References

(1) Mackay, D., A. DiGuardo, S. Paterson and C. Cowan, EQC Model ver. 1.01, 1997, available form the Emvironmental Centre, Trent Univ. Canada.

(2) Meylan, M. Syracuse Research Corporation (1994-1999) Calculation program contained in EPIWIN (Esitmate ver. 3.04) available from SRC.

(3) Wilson, A., (1996). Plasticizers - Selection, Applications and Implications. Rapra Review Reports 8:15-16.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

Chapter : Chapters 4 & 5

Remark : Because of the similarity in chemical structure, the Panel believes that the toxicological properties of the substances in this category will be similar as well. Thus, the Panel considers that the data for the best tested member of this category, tris-2-(ethylhexyl) trimellitate (TOTM), also represents the potential for human and environmental effects of the other members of this category.

TOTM has been sponsored under the OECD SIDS program through ICCA. A review of the available data for TOTM (see attached Table) indicates that all endpoints have been adequately addressed, and that TOTM exhibits a low order of toxicity.

Due to their higher molecular weight and bulky side chains, the remaining members of this category are expected to demonstrate a lower order of toxicity than TOTM. This is supported by a similar structural-activity relationship observed with phthalate ester compounds, i.e., the higher molecular weight phthalates (ester side chains >C7) are less active that the transitional phthalates (ester side chains C4-C6). Thus, the use of TOTM to represent the potential hazards of the other category members is a conservative position.

Attached doc. : Summary of SIDS Information on Trimellitates.doc

Flag : Critical study for SIDS endpoint

13.12.2001

7.3 RISK ASSESSMENT

I U C L I D

Data Set

Existing Chemical	:	ID: 3319-31-1
CAS No.	:	3319-31-1
EINECS Name	:	tris(2-ethylhexyl) benzene-1,2,4-tricarboxylate
EINECS No.	:	222-020-0
TSCA Name	:	1,2,4-Benzenetricarboxylic acid, tris(2-ethylhexyl) ester
Molecular Formula	:	C33H54O6

Producer Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	02.11.2000

Substance Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	02.11.2000
Memo	:	ACC Phthalate Esters Panel HPV Testing Group
Printing date	:	13.12.2001
Revision date	:	
Date of last Update	:	13.12.2001
Number of Pages	:	16

1.0.1 OECD AND COMPANY INFORMATION

Type	:	lead organisation
Name	:	ACC Phthalate Esters Panel HPV Testing Group
Partner	:	Dr. Marian Stanley
Date	:	
Street	:	1300 Wilson Blvd.
Town	:	22209 Arlington, VA
Country	:	United States
Phone	:	(703) 741-5623
Telefax	:	(703) 741-6091
Telex	:	
Cedex	:	
Remark	:	The American Chemistry Council Phthalate Esters Panel sponsoring this test plan includes the following member companies: Eastman Chemical Company ExxonMobil Chemical Company Sunoco Chemicals Teknor Apex Company
Flag	:	Critical study for SIDS endpoint

26.10.2001

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	organic
Physical status	:	liquid
Purity	:	% w/w

09.10.2001

1.1.0 DETAILS ON TEMPLATE

Comment

This chemical is part of the Trimellitate category. The category includes the following four CAS numbers: 3319-31-1, 27251-75-8, 53894-23-8 and 67989-23-5.

Remark

DESCRIPTION OF THE TRIMELLITATES CATEGORY

The trimellitates comprise a family of chemicals synthesized by esterifying trimellitic anhydride with alcohols with average carbon numbers ranging from approximately C7-C10, in the presence of an acid catalyst. The category includes the four trimellitates: 3319-31-1 (TOTM), 27251-75-8 (TIOTM), 53894-23-8 (TINTM), and 67989-23-5 (DOTM). Trimellitates in this category are all 1,2,4-benzenetricarboxylic acids with side chain ester groups ranging from C8 to C10. The structural formula for trimellitates varies somewhat depending on the isomeric composition of the alcohols used in their manufacture. The specific alcohols used are 2-ethylhexanol (TOTM), iso-octyl alcohol (TIOTM), iso-nonyl alcohol (TINTM), and a mixture of linear and branched decyl (40%) and octyl (60%) alcohols (DOTM).

Trimellitates are colorless to slightly yellow liquids with high boiling points (> 250oC) and low vapor pressures; properties which contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils, but essentially insoluble in water. Because of the similarity in structure as well as physicochemical

properties, the trimellitates were grouped into a single category containing four substances with carboxylic side chain ester groups ranging from C8-C10.

Flag Critical study for SIDS endpoint
09.10.2001

1.7 USE PATTERN

Type : industrial
Category : Polymers industry
Remark : Trimellitates are used predominantly as plasticizers for production of flexible PVC. Because of their relatively high molecular weight (>500 g/mole) and bulky structure, they have lower volatility and greater resistance to migration than the corresponding phthalate ester plasticizers. They are predominantly used in the manufacture of high temperature PVC cables (Wilson, 1996). Since these chemicals are produced in closed systems, there is essentially no occupational exposure to these substances except at the flexible PVC production facility. Usually, these substances have been already blended to the compound as plasticizer, so it is not expected that downstream users or consumers are directly exposed to trimellitates.
Flag : Critical study for SIDS endpoint
13.12.2001

(9)

2.1 MELTING POINT

Value	:	-46 °C
Remark	:	pour point
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(4) not assignable
20.12.2000		(7)

Value	:	97 °C
Decomposition	:	no at °C
Sublimation	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Melting point calculation by MPBPWIN ver. 1.40 using calculation methods of Joback and Gold and Ogle.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation Melting point calculation seems to give erroneously high results for this class of chemicals.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(3) invalid
16.10.2001		(8)

2.2 BOILING POINT

Value	:	541 °C at 1013 hPa
Decomposition	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Boiling point calculation by MPBPWIN ver. 1.40 using calculation method of Stein and Brown.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
16.10.2001		(8)

2.4 VAPOUR PRESSURE

Value	:	.0000000000525 hPa at 25° C
Decomposition	:	no
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Decomposition	:	no
Method	:	Vapor pressure calculation by MPBPWIN ver. 1.40 using calculation method of Grain.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

16.10.2001 (8)

Value	:	.133 hPa at 200° C
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(4) not assignable

16.10.2001 (7)

2.5 PARTITION COEFFICIENT

Log pow	:	4.35 at 25° C
Method		other (measured)
Year	:	1984
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The study was conducted following the methods outlined in the ABC protocol # A-8003 (revised 6 August, 1984) for CMA Environmental Effects Testing Program with TOTM. 0.4% solutions of TOTM (supplied by CMA) were prepared in n-octanol and 40 ml portions were shaken for 24 hours with 400 ml water. After a 48 hour settling period, aliquots from both phases were drawn to analyse their TOTM concentrations using GC or HPLC.
Source	:	Internaltional Speciality Chemicals Ltd. Hythe FMC Corporation Manchester.

16.10.2001

Log pow	:	5.94 at 25° C
Method		OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year	:	2000
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Chemicals Evaluation and Research Institute, Japan Ministry of International Trade and Industry (1998)
Reliability	:	(2) valid with restrictions

16.10.2001

Log pow	:	11.59 at 25° C
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Partition coefficient by LOGKOWWIN ver. 1.65 using an atom/fragment calculation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

30.10.2001

2.6.1 WATER SOLUBILITY

Value	:	.00005 other: ug/L at 25 ° C
Qualitative	:	
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other
Year	:	2000
GLP	:	

Test substance	:	
Method	:	Water solubility calculated using WSKOWWIN ver. 1.36 based on Kow correlation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
30.10.2001		
Value	:	.00039 mg/l at 25 ° C
Qualitative	:	of very low solubility
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	OECD Guide-line 105 "Water Solubility"
Year	:	1998
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Chemicals Evaluation and Research Institute, Japan Ministry of International Trade and Industry (1998)
16.10.2001		

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spect.	:	nm
Rel. intensity	:	1 based on Intensity of Sunlight
Conc. of subst.	:	at 25 degree C
Indirect photolysis		
Sensitizer	:	OH
Conc. of sens.	:	1500000 molecule/cm3
Rate constant	:	.00000000003277 cm3/(molecule*sec)
Degradation	:	% after
Deg. Product	:	
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Photodegradation rate calculated by AOPWIN ver. 1.89 based on the methods of Atkinson.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

20.12.2000 (8)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	.3 year at 25 degree C
t1/2 pH9	:	at degree C
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Hydrolysis rate calculated by HYDROWIN ver. 1.67 based on work for EPA by T. Mill et al.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

20.12.2000 (8)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	other
Air (level I)	:	0
Water (level I)	:	0
Soil (level I)	:	97.8
Biota (level II / III)	:	
Soil (level II / III)	:	
Method	:	other
Year	:	2000

Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
20.12.2000		(6)

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	Calculation according Mackay, Level I
Year	:	2000
Result	:	Soil - 97.8% Air - 0.00000364% Water - 0.000000284% Sediment - 2.17% Suspended sed. - 0.068%
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
20.12.2000		(6)

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	domestic sewage
Concentration	:	10mg/l related to Test substance related to
Contact time	:	28 day
Degradation	:	ca. 68.3 - 71.1 % after
Result	:	readily biodegradable
Deg. Product	:	
Method	:	other
Year	:	1985
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Method/Guideline-USEPA 1982, CO2 Evolution, Shake Flask. Domestic sewage, mixed liquor. Kinetics-Not Reported Degradation Products-Not Reported Analytical Monitoring-No
Result	:	The results of the first and third test are reported (68.3 and 71.1% biodegrdation respectively).
Test condition	:	Inoculum consisted of deionized water, mineral stocks, native soil, aerated mixed liquor and raw sewage. Inoculum was aged prior to test initiation. The test chemicals were added to flasks containing medium and inoculum. The flask were incubated and shaken in the dark for 28 days. Twelve flasks were prepared; 3 controls, 3 dextrose, 3 test substance and 3 with test substance and HgCl2 (to prevent microbial growth). The CO2 production was captured in KOH solution. 500ml Erlenmeyer flasks were used as test vessels. Test flasks were shaken at a rate of 60rpm at 25 +/- 2 deg C. Plate count at initiation was 1.7 x 105 colony/ml. The pH at initiation was not reported. Three test trials were conducted. The methods described are those of trial #3.
Test substance	:	Nominal test concentration for all substances = 10mg/L Tris (2-ethylhexyl) Trimellitate (CAS# 3319-31-1) (1,2,-benzenedicarboxylic acid, Tris (2-ethylhexyl) Ester)

Synonym: TOTM

Conclusion : The substance is readily biodegradable using mixed populations of microorganisms,

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

29.11.2000 (1)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

See attached TOTM SIAR document

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

See attached TOTM SIAR document

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

See attached TOTM SIAR document

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	male
Number of animals	:	20
Vehicle	:	other
Value	:	> 3200 mg/kg bw
Method	:	other
Year	:	1971
GLP	:	no
Test substance	:	other TS
Method	:	Rats and mice
Remark	:	No animals died. All animals gained weight post-exposure
Test condition	:	Two male rats and two male mice per dose level were treated with 200, 400, 800, 1600, or 3200 mg/kg neat test substance by oral gavage. The animals were observed for a period of 14 days for survival and body weight changes.
Test substance	:	1,2,4-benzenetricarboxylic, tris(2-ethylhexyl)ester (tri-2-ethylhexyl trimellitate)
Reliability	:	(2) valid with restrictions

28.12.2000 (4)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Species	:	rat
Strain	:	
Sex	:	no data
Number of animals	:	3
Vehicle	:	
Exposure time	:	6 hour(s)
Value	:	ca.
Method	:	other
Year	:	1971
GLP	:	no
Test substance	:	other TS
Remark	:	Three rats were exposed for 6 hours to a nominal concentration of 4.17, 2.64, or 0.23 mg/L of the test substance in a whole-body inhalation chamber. The test substance was heated to 180oC to generate the test atmosphere which was likely a mixture of aerosol and heated vapor. The animals were observed for a period of 14 days for survival.
Test condition	:	1,2,4-benzenetricarboxylic, tris(2-ethylhexyl)ester (tri-2-ethylhexyl trimellitate)
Test substance	:	Three rats were exposed for 6 hours to a nominal concentration of 4.17, 2.64, or 0.23 mg/L of the test substance in a whole-body inhalation chamber. The test substance was heated to 180oC to generate the test atmosphere which was likely a mixture of aerosol and heated vapor. The animals were observed for a period of 14 days for survival.
Conclusion	:	100% mortality at >2.64 mg/L (nominal). LC50 not determined.
Reliability	:	(2) valid with restrictions

28.12.2000 (5)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	guinea pig
Strain	:	
Sex	:	no data
Number of animals	:	3
Vehicle	:	other
Value	:	> 20 ml/kg bw
Method	:	other
Year	:	
GLP	:	no
Test substance	:	other TS
Remark	:	No animals died. Moderate to severe edema and moderate erythema were observed at 24 hours. All animals appeared normal after one week.
Test condition	:	Three guinea pigs were shaved and depilated prior to dosing. Dose levels of 5, 10, or 20 ml/kg of the neat test substance were applied to the skin (one animal per dose level) and the area wrapped with an impervious material for 24 hours. Following unwrapping, the skin was evaluated for signs of irritation. The animals were observed for a period of 14 days for survival.
Test substance	:	1,2,4-benzenetricarboxylic, tris(2-ethylhexyl)ester (tri-2-ethylhexyl trimellitate)
Conclusion	:	Under the conditions of this study, the test substance has a low order of acute dermal toxicity in rats.
Reliability	:	(2) valid with restrictions

28.12.2000 (3)

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	28 days
Frequency of treatment	:	Daily
Post obs. period	:	No
Doses	:	0, 0.2, 0.67 or 2.0% (0, 183, 654, 1734 mg/kg/day
Control group	:	yes
NOAEL	:	= .67 %
Method	:	OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year	:	1985
GLP	:	yes
Test substance	:	other TS
Method	:	Analysis of variance with significant groups compared by Least Significant Difference test ($p < 0.05$)
Remark	:	There were no statistically significant differences between the body weights of control and treated animals. Initially, there was a significant decrease in food intake for females (2%); however, food intake gradually increased throughout the study. In males, there were no treatment-related effects on food consumption. Serum albumin levels were significantly increased in males and females at the mid and high dose. Similarly, leukocyte counts were increased in both sexes at the two higher dose levels; however, this increase was significant only in males. At the two lower dose levels, hematocrit and mean cell volume decreased in female rats. In both sexes, the absolute and relative liver weights increased at the mid-dose level, but not at the highest dose. The high dose animals showed slight increases in the number but not size of peroxisomes. There were no deaths related to treatment in this study.

Test condition	:	Male and female rats were randomly assigned to various treatment groups. Following the acclimation period, rats were administered dietary doses of either the control or the test substance for 28 days. DEHP was used in this study as a reference compound. Animals were monitored twice each day. Food intake was measured from Days -3 to day 0 and continuous intakes were measured at twice-weekly intervals until the day preceding the autopsy. One day prior to autopsy, blood was collected from each animal and the following endpoints were evaluated: differential leukocyte and erythrocyte counts, mean cell volume, packed cell volume, total leukocyte count, platelet count and reticulocyte count. Serum chemistry analysis of several endpoints was also performed. On the day of sacrifice, the following organs were retained in 10% neutral buffered formalin: cecum, colon, pancreas, prostate, skeletal muscle, small intestine, stomach, thymus, and uterus. Two slices of liver were subjected to electron microscopy for evaluation of peroxisome proliferation.
Test substance	:	1,2,4-benzenetricarboxylic, tris(2-ethylhexyl)ester (tri-2-ethylhexyl trimellitate)
Conclusion	:	The test substance caused a slight peroxisome proliferation at the high dose but was less potent than comparable doses of DEHP.
Reliability	:	(1) valid without restriction
28.12.2000		

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Bacterial
Concentration	:	100, 333, 1000, 3333, 10000 mg/ml.
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year	:	1988
GLP	:	yes
Test substance	:	other TS
Method	:	Chemicals were judged to be mutagenic if the test results produced a dose-related, reproducible increase in histidine revertants over control. It was not a requirement for mutagenic responses to reach two-fold over background.
Test condition	:	Prior to assay initiation, a toxicity pretest was performed using tester strain TA100. Based on these results, the doses for the final assay were determined. In the definitive assay, each of the five strains was dosed with either the test substance; a vehicle control (DMSO); or a nontreated control and a positive control. The test mixture containing the tester strain and test substance with or without S9 was added to the surface of petri dishes containing Vogel-Bonner medium. The histidine-independent colonies that formed on the plates were counted following a two-day incubation at 37°C. Positive controls were as follows: 2-aminoanthracene (all strains with S9); sodium azide (without S9, TA1535, TA100), 4-nitro-o-phenylenediamine (without S9, TA98) and 9-aminoacridine (without S9, TA 97, TA1537). There were 3 plates/dose group/strain/treatment. The test results were verified by repeating the assay. If the results were negative, they were repeated first without S9 and then with 30% S9.
Test substance	:	1,2,4-benzenetricarboxylic, tris(2-ethylhexyl)ester (tri-2-ethylhexyl trimellitate)
Conclusion	:	Under the conditions of this study, tri (2-ethylhexyl) trimellitate was not mutagenic at doses up to 10,000 mg/ml.
Reliability	:	(1) valid without restriction
28.12.2000		(2)

5.8 TOXICITY TO REPRODUCTION

See attached TOTM SIAR document

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

See attached TOTM SIAR document

5.10 OTHER RELEVANT INFORMATION

See attached TOTM SIAR document

(1) ABC Final Report, # 31891, Shake Flask Biodegradation of 14C-Tris (2-ethylhexyl) Trimellitate (TOTM). 1986, Sponsored by CMA. Performed by: ABC Laboratories Columbia, MO.

(2) E. Zeiger, B. Anderson, S. Haworth, T. Lawlor and K. Mortelmans. (1988). Salmonella mutagenicity tests. IV. Results from the testing of 300 chemicals. Environmental and Molecular Mutagenesis 11(12):1-158 .

(3) Eastman Kodak Company (1971). Tri(2-ethylhexyl)trimellitate. Acute dermal toxicity. Unpublished report.

(4) Eastman Kodak Company (1971). Tri(2-ethylhexyl)trimellitate. Acute oral toxicity. Unpublished report.

(5) Eastman Kodak Company (1971). Tri(2-ethylhexyl)trimellitate. Acute inhalation toxicity. Unpublished report.

(6) Mackay, D., A. DiGuardo, S. Paterson and C. Cowan, EQC Model ver. 1.01, 1997, available form the Emvironmental Centre, Trent Univ. Canada.

(7) Manufacturer Safety Data Sheet

(8) Meylan, M. Syracuse Research Corporation (1994-1999) Calculation program contained in EPIWIN (Esitmate ver. 3.04) available from SRC.

(9) Wilson, A., (1996). Plasticizers - Selection, Applications and Implications. Rapra Review Reports 8:15-16.

7.2 HAZARD SUMMARY

Chapter : Chapters 4 & 5
Remark : Because of the similarity in chemical structure, the Panel believes that the toxicological properties of the substances in this category will be similar as well. Thus, the Panel considers that the data for the best tested member of this category, tris-2-(ethylhexyl) trimellitate (TOTM), also represents the potential for human and environmental effects of the other members of this category.

TOTM has been sponsored under the OECD SIDS program through ICCA. A review of the available data for TOTM (see attached Table) indicates that all endpoints have been adequately addressed, and that TOTM exhibits a low order of toxicity.

Due to their higher molecular weight and bulky side chains, the remaining members of this category are expected to demonstrate a lower order of toxicity than TOTM. This is supported by a similar structural-activity relationship observed with phthalate ester compounds, i.e., the higher molecular weight phthalates (ester side chains >C7) are less active that the transitional phthalates (ester side chains C4-C6). Thus, the use of TOTM to represent the potential hazards of the other category members is a conservative position.

Attached doc. : Summary of SIDS Information on Trimellitates.doc
Flag : Critical study for SIDS endpoint
13.12.2001

7.3 RISK ASSESSMENT

Memo : SIDS Initial Assessment Profile (SIAP), SIDS Initial Assessment Report (SIAR) and Robust Summary for TOTM -- submitted by Japan under ICCA HPV program.
Attached doc. : TOTM_SIAR.pdf
Flag : Critical study for SIDS endpoint
13.12.2001

Summary of SIDS Information on Trimellitates
A. Physical/Chemical Properties of Trimellitates

(R) Carbon Chain Length	CAS Number	Chemical Name	MP* (°C)	BP** (°C)	VP (hPa@25°C)	PC (log Pow)	Water Solubility (mg/L @25°C)	Photodeg Half-life (days)	Hydrolysis Half-life (yrs)	Transport (%) c			
										Soil	Air	Water	Sediment
C8	3319-31-1	tris 2-ethylhexyl (TOTM)	-46 97 c	>300 541 c	<0.0001*** 5.25E-11 c	5.94 11.59 c	3.9E-04 4.51E-08 c	0.33 c	0.05 0.32 c	97.8	3.6E - 6	2.8E - 7	2.17
C8	27251-75-8	triisooctyl ester	<0 197 c	541 c	5.25E-11 c	11.59 c	4.51E-08 c	0.35 c	0.43 c	97.8	3.64E - 6	2.8E - 7	2.17
C9	53894-23-8	triisononyl ester	<0 224 c	>300 575 c	3.17E-12 c	13.06 c	1.32E-09 c	0.31 c	0.86 c	97.8	2.74E - 7	9.61E -9	2.17
C8,C10	67989-23-5	decyl, octyl ester	<0 234 c	585 c	1.37E-12 c	12.79 c	2.78E-09 c	0.32 c	0.98 c	97.8	1.02E - 7	1.79E - 8	2.17

c = calculated data using EPWIN; all other values are derived from measurements

* = All of these trimellitates are liquids at zero degrees C. Modeled data do not accurately reflect melting points for these substances

** = Measured boiling points were determined to be >300°C at 0.66 kPa

*** = vapor pressure of TOTM 13 Pa @ 200°C

Summary of SIDS Information on Trimellitates
B. Toxicology Data on Trimellitates

(R) Carbon Chain Length	CAS Number	Chemical Name	Acute Oral LD50	Acute Dermal LD50	Acute Inhalation LC50	Repeated Dose Toxicity	GeneTox (Ames)	GeneTox (Chrom. Abs.)	Toxicity to Reproduction	Developmental Toxicity / Teratogenicity	Acute Fish (A) mg/L	Daphnia (B) mg/L	Algal (C) mg/L	Biodegradation %
C8	3319-31-1	tris 2-ethylhexyl (TOTM)	> 3.2 g/kg (rat, mouse)	>20 ml/kg (guinea pig) >2.0 ml/kg (rabbit)	<2.64 mg/L (rat, nominal)	NOAEL (rat, dietary) 654 mg/kg/day	Negative	Negative (CHL/IU cells)	NOAEL (rat, oral) 1000 mg/kg/day	NOAEL (rat, oral) 1000 mg/kg/day (3)	>100	>180	>100	68-71 (1) 4.2 (2)
C8	27251-75-8	Triisooctyl ester												
C9	53894-23-8	Triisononyl ester	> 10 g/kg (rat)											
C8, C10	67989-23-5	decyl, octyl ester												

Footnotes: A) Japanese Medaka (*Oryzias latipes*), 96 hr LC50 & NOEC
B) *Daphnia magna*, 48-hr EC50
C) *Selenastrum capricornutum*, 72-hr EC50 & NOEC

(1) Inherent biodegradation by Shake Flask Method
(2) Ready biodegradation by MITI method (OECD 301C)
(3) OECD Preliminary reproduction toxicity screening test; indirect measure of develomental effects

I U C L I D

Data Set

Existing Chemical	:	ID: 27251-75-8
CAS No.	:	27251-75-8
TSCA Name	:	1,2,4-benzenetricarboxcylic acid, triisooctyl ester
Generic name	:	triisooctyl ester trimellitate

Producer Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	26.10.2000

Substance Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	26.10.2000
Memo	:	ACC Phthalate Esters HPV Panel
Printing date	:	13.12.2001
Revision date	:	
Date of last Update	:	30.10.2001
Number of Pages	:	11
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 OECD AND COMPANY INFORMATION

Type	:	lead organisation
Name	:	ACC Phthalate Esters Panel HPV Testing Group
Partner	:	Dr. Marian Stanley
Date	:	
Street	:	1300 Wilson Blvd.
Town	:	22209 Arlington, VA
Country	:	United States
Phone	:	(703) 741-5623
Telefax	:	(703) 741-6091
Telex	:	
Cedex	:	
Remark	:	The American Chemistry Council Phthalate Esters Panel sponsoring this test plan includes the following member companies: Eastman Chemical Company ExxonMobil Chemical Company Sunoco Chemicals Teknor Apex Company
Flag	:	Critical study for SIDS endpoint

26.10.2001

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	organic
Physical status	:	liquid
Purity	:	% w/w

09.10.2001

1.1.0 DETAILS ON TEMPLATE

Comment

This chemical is part of the Trimellitate category. The category includes the following four CAS numbers: 3319-31-1, 27251-75-8, 53894-23-8 and 67989-23-5.

Remark

DESCRIPTION OF THE TRIMELLITATES CATEGORY

The trimellitates comprise a family of chemicals synthesized by esterifying trimellitic anhydride with alcohols with average carbon numbers ranging from approximately C7-C10, in the presence of an acid catalyst. The category includes the four trimellitates: 3319-31-1 (TOTM), 27251-75-8 (TIOTM),
53894-23-8 (TINTM), and 67989-23-5 (DOTM). Trimellitates in this category are all 1,2,4-benzenetricarboxylic acids with side chain ester groups ranging from C8 to C10. The structural formula for trimellitates varies somewhat depending on the isomeric composition of the alcohols used in their manufacture. The specific alcohols used are 2-ethylhexanol (TOTM), iso-octyl alcohol (TIOTM), iso-nonyl alcohol (TINTM), and a mixture of linear and branched decyl (40%) and octyl (60%) alcohols (DOTM).

Trimellitates are colorless to slightly yellow liquids with high boiling points (> 250oC) and low vapor pressures; properties which contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils, but essentially insoluble in

water. Because of the similarity in structure as well as physicochemical properties, the trimellitates were grouped into a single category containing four substances with carboxylic side chain ester groups ranging from C8-C10.

Flag Critical study for SIDS endpoint
09.10.2001

1.7 USE PATTERN

Type : industrial
Category : Polymers industry
Remark : Trimellitates are used predominantly as plasticizers for production of flexible PVC. Because of their relatively high molecular weight (>500 g/mole) and bulky structure, they have lower volatility and greater resistance to migration than the corresponding phthalate ester plasticizers. They are predominantly used in the manufacture of high temperature PVC cables (Wilson, 1996). Since these chemicals are produced in closed systems, there is essentially no occupational exposure to these substances except at the flexible PVC production facility. Usually, these substances have been already blended to the compound as plasticizer, so it is not expected that downstream users or consumers are directly exposed to trimellitates.
Flag : Critical study for SIDS endpoint
13.12.2001

(3)

2.1 MELTING POINT

Value	:	= 197 °C
Decomposition	:	no at °C
Sublimation	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Melting point calculation by MPBPWIN ver. 1.40 using calculation methods of Joback and Gold and Ogle.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation. Melting point calculation seems to give erroneously high results for the this class of chemicals.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(3) invalid

29.10.2001 (2)

2.2 BOILING POINT

Value	:	= 541 °C at 1013 hPa
Decomposition	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Boiling point calculation by MPBPWIN ver. 1.40 using calculation method of Stein and Brown.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

2.4 VAPOUR PRESSURE

Value	:	= .0000000000524 hPa at 25° C
Decomposition	:	no
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Decomposition	:	no
Method	:	Vapor pressure calculation by MPBPWIN ver. 1.40 using calculation method of Grain.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

2.5 PARTITION COEFFICIENT

Log pow	:	= 11.59 at 25° C
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Partition coefficient by LOGKOWWIN ver. 1.65 using an atom/fragment calculation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

2.6.1 WATER SOLUBILITY

Value	:	.00005 other: ug/L at 25 ° C
Qualitative	:	
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other: calculated
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Water solubility calculated using WSKOWWIN ver. 1.36 based on Kow correlation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

30.10.2001

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spect.	:	nm
Rel. intensity	:	1 based on Intensity of Sunlight
Conc. of subst.	:	at 25 degree C
Indirect photolysis		
Sensitizer	:	OH
Conc. of sens.	:	1500000 molecule/cm3
Rate constant	:	.00000000003068 cm3/(molecule*sec)
Degradation	:	% after
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Photodegradation rate calculated by AOPWIN ver. 1.89 based on the methods of Atkinson.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	.4 year at 25 degree C
t1/2 pH9	:	at degree C
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Hydrolysis rate calculated by HYDROWIN ver. 1.67 based on work for EPA by T. Mill et al.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	other
Air (level I)	:	0
Water (level I)	:	0
Soil (level I)	:	97.8
Biota (level II / III)	:	
Soil (level II / III)	:	
Method	:	other
Year	:	2000

Source : ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability : (2) valid with restrictions
20.12.2000 (1)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year : 2000
Result : Soil - 97.8%
Air - 0.00000364%
Water - 0.000000284%
Sediment - 2.17%
Suspended sed. - 0.068%
Source : ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability : (2) valid with restrictions
20.12.2000 (1)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(1) Mackay, D., A. DiGuardo, S. Paterson and C. Cowan, EQC Model ver. 1.01, 1997, available form the Emvironmental Centre, Trent Univ. Canada.

(2) Meylan, M. Syracuse Research Corporation (1994-1999) Calculation program contained in EPIWIN (Esitmate ver. 3.04) available from SRC.

(3) Wilson, A., (1996). Plasticizers - Selection, Applications and Implications. Rapra Review Reports 8:15-16.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

Chapter : Chapters 4 & 5

Remark : Because of the similarity in chemical structure, the Panel believes that the toxicological properties of the substances in this category will be similar as well. Thus, the Panel considers that the data for the best tested member of this category, tris-2-(ethylhexyl) trimellitate (TOTM), also represents the potential for human and environmental effects of the other members of this category.

TOTM has been sponsored under the OECD SIDS program through ICCA. A review of the available data for TOTM (see attached Table) indicates that all endpoints have been adequately addressed, and that TOTM exhibits a low order of toxicity.

Due to their higher molecular weight and bulky side chains, the remaining members of this category are expected to demonstrate a lower order of toxicity than TOTM. This is supported by a similar structural-activity relationship observed with phthalate ester compounds, i.e., the higher molecular weight phthalates (ester side chains >C7) are less active that the transitional phthalates (ester side chains C4-C6). Thus, the use of TOTM to represent the potential hazards of the other category members is a conservative position.

Attached doc. : Summary of SIDS Information on Trimellitates.doc

Flag : Critical study for SIDS endpoint

13.12.2001

7.3 RISK ASSESSMENT

I U C L I D

Data Set

Existing Chemical	:	ID: 27251-75-8
CAS No.	:	27251-75-8
TSCA Name	:	1,2,4-benzenetricarboxcylic acid, triisooctyl ester
Generic name	:	triisooctyl ester trimellitate

Producer Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	26.10.2000

Substance Related Part

Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	26.10.2000
Memo	:	ACC Phthalate Esters HPV Panel
Printing date	:	13.12.2001
Revision date	:	
Date of last Update	:	30.10.2001
Number of Pages	:	11

1.0.1 OECD AND COMPANY INFORMATION

Type	:	lead organisation
Name	:	ACC Phthalate Esters Panel HPV Testing Group
Partner	:	Dr. Marian Stanley
Date	:	
Street	:	1300 Wilson Blvd.
Town	:	22209 Arlington, VA
Country	:	United States
Phone	:	(703) 741-5623
Telefax	:	(703) 741-6091
Telex	:	
Cedex	:	
Remark	:	The American Chemistry Council Phthalate Esters Panel sponsoring this test plan includes the following member companies: Eastman Chemical Company ExxonMobil Chemical Company Sunoco Chemicals Teknor Apex Company
Flag	:	Critical study for SIDS endpoint

26.10.2001

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	organic
Physical status	:	liquid
Purity	:	% w/w

09.10.2001

1.1.0 DETAILS ON TEMPLATE

Comment

This chemical is part of the Trimellitate category. The category includes the following four CAS numbers: 3319-31-1, 27251-75-8, 53894-23-8 and 67989-23-5.

Remark

DESCRIPTION OF THE TRIMELLITATES CATEGORY

The trimellitates comprise a family of chemicals synthesized by esterifying trimellitic anhydride with alcohols with average carbon numbers ranging from approximately C7-C10, in the presence of an acid catalyst. The category includes the four trimellitates: 3319-31-1 (TOTM), 27251-75-8 (TIOTM),
53894-23-8 (TINTM), and 67989-23-5 (DOTM). Trimellitates in this category are all 1,2,4-benzenetricarboxylic acids with side chain ester groups ranging from C8 to C10. The structural formula for trimellitates varies somewhat depending on the isomeric composition of the alcohols used in their manufacture. The specific alcohols used are 2-ethylhexanol (TOTM), iso-octyl alcohol (TIOTM), iso-nonyl alcohol (TINTM), and a mixture of linear and branched decyl (40%) and octyl (60%) alcohols (DOTM).

Trimellitates are colorless to slightly yellow liquids with high boiling points (> 250oC) and low vapor pressures; properties which contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils, but essentially insoluble in

water. Because of the similarity in structure as well as physicochemical properties, the trimellitates were grouped into a single category containing four substances with carboxylic side chain ester groups ranging from C8-C10.

Flag Critical study for SIDS endpoint
09.10.2001

1.7 USE PATTERN

Type	:	industrial
Category	:	Polymers industry
Remark	:	Trimellitates are used predominantly as plasticizers for production of flexible PVC. Because of their relatively high molecular weight (>500 g/mole) and bulky structure, they have lower volatility and greater resistance to migration than the corresponding phthalate ester plasticizers. They are predominantly used in the manufacture of high temperature PVC cables (Wilson, 1996). Since these chemicals are produced in closed systems, there is essentially no occupational exposure to these substances except at the flexible PVC production facility. Usually, these substances have been already blended to the compound as plasticizer, so it is not expected that downstream users or consumers are directly exposed to trimellitates.
Flag	:	Critical study for SIDS endpoint

13.12.2001 (3)

2.1 MELTING POINT

Value	:	= 197 °C
Decomposition	:	no at °C
Sublimation	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Melting point calculation by MPBPWIN ver. 1.40 using calculation methods of Joback and Gold and Ogle.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation. Melting point calculation seems to give erroneously high results for the this class of chemicals.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(3) invalid

29.10.2001 (2)

2.2 BOILING POINT

Value	:	= 541 °C at 1013 hPa
Decomposition	:	no
Method	:	other
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Boiling point calculation by MPBPWIN ver. 1.40 using calculation method of Stein and Brown.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

2.4 VAPOUR PRESSURE

Value	:	= .0000000000524 hPa at 25° C
Decomposition	:	no
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Decomposition	:	no
Method	:	Vapor pressure calculation by MPBPWIN ver. 1.40 using calculation method of Grain.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

2.5 PARTITION COEFFICIENT

Log pow	:	= 11.59 at 25° C
Method		other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Partition coefficient by LOGKOWWIN ver. 1.65 using an atom/fragment calculation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

2.6.1 WATER SOLUBILITY

Value	:	.00005 other: ug/L at 25 ° C
Qualitative	:	
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other: calculated
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Water solubility calculated using WSKOWWIN ver. 1.36 based on Kow correlation method of Meylan and Howard.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

30.10.2001

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spect.	:	nm
Rel. intensity	:	1 based on Intensity of Sunlight
Conc. of subst.	:	at 25 degree C
Indirect photolysis		
Sensitizer	:	OH
Conc. of sens.	:	1500000 molecule/cm3
Rate constant	:	.00000000003068 cm3/(molecule*sec)
Degradation	:	% after
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Photodegradation rate calculated by AOPWIN ver. 1.89 based on the methods of Atkinson.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	.4 year at 25 degree C
t1/2 pH9	:	at degree C
Deg. Product	:	not measured
Method	:	other (calculated)
Year	:	2000
GLP	:	
Test substance	:	
Method	:	Hydrolysis rate calculated by HYDROWIN ver. 1.67 based on work for EPA by T. Mill et al.
Remark	:	EPIWIN is used and advocated by the US EPA for chemical property estimation.
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions

29.10.2001 (2)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	other
Air (level I)	:	0
Water (level I)	:	0
Soil (level I)	:	97.8
Biota (level II / III)	:	
Soil (level II / III)	:	
Method	:	other
Year	:	2000

Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
20.12.2000		(1)

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	Calculation according Mackay, Level I
Year	:	2000
Result	:	Soil - 97.8% Air - 0.00000364% Water - 0.000000284% Sediment - 2.17% Suspended sed. - 0.068%
Source	:	ExxonMobil Biomedical Sciences, Inc. Annandale, N.J. USA
Reliability	:	(2) valid with restrictions
20.12.2000		(1)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

6. References

(1) Mackay, D., A. DiGuardo, S. Paterson and C. Cowan, EQC Model ver. 1.01, 1997, available form the Emvironmental Centre, Trent Univ. Canada.

(2) Meylan, M. Syracuse Research Corporation (1994-1999) Calculation program contained in EPIWIN (Esitmate ver. 3.04) available from SRC.

(3) Wilson, A., (1996). Plasticizers - Selection, Applications and Implications. Rapra Review Reports 8:15-16.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

Chapter : Chapters 4 & 5

Remark : Because of the similarity in chemical structure, the Panel believes that the toxicological properties of the substances in this category will be similar as well. Thus, the Panel considers that the data for the best tested member of this category, tris-2-(ethylhexyl) trimellitate (TOTM), also represents the potential for human and environmental effects of the other members of this category.

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Attached doc. : Summary of SIDS Information on Trimellitates.doc

Flag : Critical study for SIDS endpoint

13.12.2001

7.3 RISK ASSESSMENT